

Defence and Technology in Europe and Elsewhere

IF the declarations of the Soviet Union and the United States are to be taken seriously, there will be a serious attempt to hold a conference on European security before the end of 1973. It remains something of a puzzle to know precisely what the conference will talk about. The project is, of course, one of those on which the Soviet Union and other Eastern European countries have set their hearts, and it is only natural that the United States should have agreed, as part of its package deal at the SALT negotiations, that the time has come when such a conference would do less harm than had originally been feared. All along, the United States has been anxious that one consequence of a conference on European security would be a further weakening of NATO, and indeed there is bound, this time next year, to be a renewal of demands from the East that the United States should be less directly involved in the defence of Western Europe. By that time, it is entirely possible that the United States itself will be willing, even eager, to reduce its commitment to the defence of other countries. "Come home, America," is likely to be Senator George McGovern's most permanent influence on 1973. And there is of course no doubt that the successful conclusion of the first stage of the SALT negotiations has quite properly encouraged hopes that other agreements will quickly follow.

Within Europe, it is inevitable that the coming decade will see a transformation of present patterns of defence. The technological developments of the past few years are a sufficient guarantee of that. As things stand, however, the NATO forces in central Europe are substantially outnumbered by the forces of the Warsaw Pact in East Germany, Poland and Czechoslovakia. In its annual report on present arrangements for defence, the International Institute of Strategic Studies estimates that 540,000 front-line troops in West Germany, Belgium and the Netherlands are opposed by 800,000 across the frontier with the German Democratic Republic (*The Military Balance 1972-73*, IISS, £0.65). Of this total, American forces account for just over a quarter. But the simple head count is to some extent misleading because it leaves out of account the armed services of France (which withdrew from NATO in 1966 but which still has two divisions stationed in Germany). It is also fair to say that the NATO forces in the outer parts of mainland Europe, Italy, Greece and Turkey for example, outnumber those in Bulgaria, Hungary and Roumania, although, by all accounts, they are less well supplied with combat tanks and aircraft than are the forces of the Warsaw Pact. Nevertheless, the present state of military preparedness in mainland Europe is a telling illustration of how the NATO countries have come to rely on military technology as a means of making up for the numerical inferiority of their forces. And although the United States makes a comparatively small contribution to the strength of the armed services, the techno-

logy on which Western Europe has come to rely is largely American in origin.

What changes can be foreseen for the years ahead? Especially now that the United States has decided to abandon the draft in July next year, it is probable that the numbers of American soldiers in Europe will be reduced, and the chances are that the recent reorganization of the US Army's divisional structure will facilitate the trend. It is inevitable that the countries of Western Europe will seek to redress the balance by the improvement of their military technology. One development already foreseen is the replacement of the missile systems which at present carry tactical nuclear warheads, known as Honest John and Sergeant, by a system known as Lance which is at once more mobile, more flexible, more accurate and of longer range. So long as short-range nuclear missiles play a part in European preparations for defence, the nations of Western Europe are likely to be anxious to re-equip their forces with the new system, recognizing as they do so that the warheads themselves will have to remain indefinitely under American control. As things stand at present, however, the NATO countries are over-supplied with nuclear weapons for tactical use. It has been estimated that the United States maintains at least 7,000 nuclear warheads in Europe, more than enough for any conceivable purpose. By contrast, the Warsaw Pact countries have fewer than a thousand tactical missiles deployed with their ground forces (and an unknown number at the disposal of their combat aircraft). Especially now that the improved Lance is likely to make possible a reduction of the numbers deployed in the West, this is plainly a field in which there is room for compromise and agreement at the European Security Conference.

The philosophy of the deployment of tactical nuclear weapons in Europe is that they are the most effective means of giving pause to an enemy attack with conventional forces, but this assumption is likely to be weakened by other developments in military technology—improved anti-tank guns, the increasing sophistication of anti-tank missiles, the use of helicopters as a defence against tanks and even the development of small and portable mines which can be used as a means of stopping tanks dead in

Price of *Nature*

The publishers of *Nature* regret that from January 1, 1973, the price of *Nature* subscriptions will be increased to £16, except for subscribers in the United States and Canada. This is the first increase of price since 1965, since when printing costs have increased by well over fifty per cent.

From the beginning of 1973, it will also be possible for readers to subscribe to *Nature Physical Science* and *Nature New Biology* separately from the Friday edition of *Nature*, but the linked subscription scheme now in force will still be available to those wishing to receive two or three of the weekly editions.



their tracks. One consequence is that the cost of developing tanks with a reasonable hope of survival on a modern battlefield is much greater than it used to be—£100,000 is now almost a starting price for a combat tank. The result is that, given the necessarily limited sums of money which the armed forces of the East and the West have at their disposal, the balance of advantage has swung decisively in favour of ground defence against incursion from either side. This is another reason for thinking that the conference next year could lay the foundations for an agreement to limit the deployment of nuclear weapons in Europe. And if both sides can be persuaded that techniques for defence against the kinds of incursions which are most likely in Europe are now more efficient than they have ever been, with the implicit understanding that a major attack by either side would bring the strategic forces of the super-powers into action, there is at least a chance that the conference will persuade both sides of the inutility of being armed to the teeth.

The consequences—and the opportunities—for Western Europe are important. Whether or not American forces in Europe are significantly reduced in the years ahead, it should be possible for Britain and the mainland countries to work out a system of defence which is at once more effective (because of the new technology), no more expensive than at present and less dependent on nuclear weapons with their inescapably bellicose connotations. But tactical nuclear weapons, whether intended for delivery by missile or aircraft, will no doubt remain, and there is a strong case for thinking that at least a part of the American role as custodian of nuclear warheads in Europe should in future be taken over by the British and the French. That is an issue which the British government should have raised long before this. In the long run, it might be a means of persuading the French of the folly of their pursuit of an independent defence policy. At the same time, there is an urgent need that defence procurement of all kinds in Western Europe should be tightly coordinated—indeed, there is now a strong case for nothing less than the full integration of the strategic defences of Western Europe. Indeed, it cannot be long before the question is raised of integrated armed forces in Western Europe, with all the touchy questions that would follow, such as the use of non-British troops in Northern Ireland. Although on the face of things, such an integration might seem to the Warsaw Pact countries to be a threat, its real significance would be the opposite. For everybody would gain from a more rational and coherent policy on the defence of Western Europe. That is another point to be made at the conference next year.

Licence for Mediocrity?

BRITAIN is to have commercial radio next year, a half century after North America and nearly two decades after it has had commercial television itself. The new radio system will begin with five stations next year and grow eventually to sixty. Unfortunately the dominant influence in the shaping of commercial radio seems to have been a desire to avoid the mistakes of the past rather than to develop the possibilities of the medium. Commercial radio will not be allowed to be a licence to print money nor will it be a surrender of scarce natural resources, the

air waves, to private investors.

The Independent Broadcasting Authority will charge very heavy rentals for the use of the air waves and for the transmission services it will build and supply to the radio stations. In the first year, rentals will range from a low of £75,000 for Birmingham's station, which is expected to reach a potential audience of 1.7 million, to £315,000 for the general entertainment station allotted to London with a potential audience of 9.2 million. These rentals will rise substantially in each of the next two years. The IBA, moreover, will siphon off 25 per cent of profits when they exceed five per cent (and 50 per cent when they exceed ten per cent) of net advertising revenue.

Yet the need to curb excess profit is only half the lesson of the past. What should be laid down in advance, and have not been, are formal requirements for programmes of high quality and local character, as well as the measures by which the IBA will compel a station to improve its performance if it falters. Not that the IBA underestimates the need for schedules that include news and educational, cultural and children's material. (The requirement is written into the Sound Broadcasting Act of 1972.) But the IBA has not fashioned any instrument of policy to ensure that this goal is achieved. Unlike its approach to matters of finance, in matters of programming the IBA is willing to proceed *ad hoc*.

When the applicants come along after December 8, the IBA will listen carefully to what they promise in the line of programmes, and contracts will go to those who best promise diversity and quality. But what will the authority do if these then are not forthcoming? The notorious reshuffling of commercial television contracts in 1967 did little to raise television programming standards. The glowing promises were not, and in some cases could not, be made good and little could be done about it.

The IBA would not be out of place to issue some general rules about the public right to access to the air waves and the need for news, current affairs and live discussions during the most desirable broadcasting hours while the applicants are still drawing up their plans. Once a style of broadcasting is established—and it sets quickly—it is nearly impossible to change it, while changes in tax levies, as the commercial television companies know, can be adjusted overnight.

It might have been better to leave the financial regulations, on the other hand, more fluid until some actual operating evidence was in hand. American experience has shown that radio is not the certain gold mine that television is. The initial high rentals may be essential, as the IBA insists, to help repay the government's loan of £2 million and to pay the radio authority's own costs. But they will shape the character of what is to come in a way that might better have been avoided. Some desirable applicants for licences may be frightened away, leaving the field to more conventional, solidly financed contenders. Advertising rates will have to be high, discouraging the small local advertisements which have value as information and are one of the great benefits to be achieved by local radio. And obviously the new stations will have to pursue the mass audience in order to justify their high advertising rates.

The unique policy instrument that the IBA has made—the secondary rental to be assessed on profits—will ingeniously keep profits within the radio system instead of being fed straight to the Treasury as they are from the

television stations. But the IBA plans to use the money itself to smooth over any inconsistencies in quality in the radio system and in particular it hopes to sponsor live performances of music. It will then be in the position of foisting balance and culture upon the stations when it should be developing the means of demanding that they produce it themselves.

Systems Analysis

THE announcement from the Royal Society and eleven other national academies of science that there is to be an International Institute of Applied Systems Analysis at Vienna (see page 361) does at least resolve the question that has perplexed those working in this and related fields since 1968, when the institute was first proposed—will it ever see the light of day? The answer is yes. The fact that the Soviet Academy of Sciences has in the last resort come forward not merely with enthusiasm but with the offer of \$1 million a year towards the budget has no doubt helped to decide the issue. In other international organizations, those linked with the United Nations for example, the Soviet government is usually unwilling to match the contributions of the United States as it has done on this occasion. And given the decision that the institute should be set up, it is of course entirely proper that it should be sited in Vienna, that there should be a director from the United States and that his deputy should be a Russian. Such difficulties as there are stem almost entirely from questions about the function of the new organization. What tasks will the international institute tackle, how well grounded will be its data? How relevant will be its analyses to contemporary problems?

The techniques of objective systems analysis must in due course have an important contribution to make to the understanding of society. The idea is that the parameters which describe the condition of society at any time may be likened to those describing the state of a political system, from which it would appear to follow that the evolution of a social system can be calculated once the starting conditions have been specified and that the effects of external changes, deliberate or otherwise, can be calculated. This, in a crude fashion, is what the Club of Rome's computer study of the whole world has attempted in *The Limits to Growth*. It is, however, plain that there are many ways in which the analysis of social systems is more complicated and necessarily more uncertain than the analysis of physical systems, where the relationships between one parameter and another can often be derived analytically from physical laws. In the more complicated real world, as those who have tried to apply systems analysis to national economies have discovered, the relationships between variables, if known at all, are at best empirical and often unpredictably dependent on unquantifiable attributes of the condition of society such as what is known as business confidence or the political mood of a nation. It follows that one of the methodological issues that must be central to the work of the International Institute of Applied Systems Analysis is the identification of those relationships which are so unsure that the applicability of the technique must itself be doubtful. The difficulty is that this is a task in which social scientists have as big a part to play as systems analysts pure and simple.

A second more practical difficulty is that of knowing where to start. This week's announcement says that the institute may well attempt to cut its teeth on a study of the evolution of the supply and the demand for energy in the years ahead. In the past few months, this has been a widespread preoccupation, especially in the United States where the Ford Foundation has set up a task force to make a study of the domestic problem. Even in this apparently quantifiable field, however, there are serious problems to watch out for. It may seem comparatively easy to relate the demand for energy with various indices of output by the manufacturing industries, but experience in countries such as Britain in recent years shows how difficult even such a limited task may be—in the 1960s, increases of efficiency in the use of energy (as well as a slackening of the pace of growth in manufacturing industry) conspired to undercut forward estimates of energy demand. There are bound also to be immense uncertainties about the future price of fuels of various kinds. In the petroleum market, for example, calculations of the relationship between the continued exploitation of known reserves and the market price, theoretically quite possible, are likely to be overridden by non-technical considerations such as the determination of the OPEC countries to put up their price. In much the same way, prices in the uranium market may depend critically on the speed with which fast reactors are brought into service—the slower, the greater will be the demand for natural uranium in the 1980s. It follows that the contribution of the International Institute of Applied Systems Analysis to a better understanding of the problem of energy supply and demand in the world as a whole may consist chiefly of a statement of the uncertainties with which calculations like these are necessarily plagued. That, if done properly, will be a public service and a spur to further understanding but not, at least, in the popular sense, a solution to any problem.

100 Years Ago



At the last meeting of the Council of the Pharmaceutical Society, it was resolved unanimously that the resolution passed in 1862, prohibiting ladies from attending the lectures, be rescinded, and that ladies be admitted as students to the lecture classes of the Society. At present but one lady has taken advantage of the privilege offered; but as soon as the resolution becomes more widely known it is probable that the liberality of the Society will be recognised by ladies, who will avail themselves of this excellent opportunity of studying practical chemistry and botany. The lectures on chemistry are by Prof. Redwood; those on botany by Prof. Bentley, commencing early in October. The chemical lectures are continued three days a week until the end of July; the botanical lectures, lasting for the same period, being delivered on two days in the week. During the summer months they are delivered in the Botanical Gardens, Regent's Park.

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OLD WORLD

European Physical Society in Need of Money

by our Special Correspondent, Wiesbaden

THE European Physical Society, now in its fifth year, is healthy in spirit but short of money. That was the message delivered by Professor H. B. G. Casimir, president of the EPS, at the society's general conference here last week.

Professor Casimir feels confident, however, that the financial problems will be surmounted and he mentioned that an organization, whose identity he could not reveal but which "would not offend anybody", is setting up a fund for the EPS worth between SF 20,000 and SF 30,000 a year for financing travel for university lecturers to and from Europe and within Europe. Such a fund is welcome but will not solve the immediate problems of the society.

Professor Casimir added that it would not be in anyone's interest for the EPS to be declared bankrupt. The society now has nine lively divisions, and two of the conferences which it sponsored recently—the one on condensed matter held in Florence and the one on computers in physics held at CERN—were particularly successful.

The fortunes of the EPS were under special scrutiny last week at the second general assembly of the society. The first general assembly was held during the society's inaugural meeting in Florence in 1969, so the Wiesbaden meeting was the first opportunity for the members to discuss as a body the way the society has progressed since its inception.

In his presidential address Professor Casimir said that the EPS has to maintain a balance between the ordinary members (in the form of the appropriate national bodies like the Institute of Physics and the German Physical Society), the individual ordinary members and the associate members, which comprise companies and laboratories whose activities, in the words of the constitution of the EPS, are "directed towards the cultural enrichment of modern society". If a balance is not maintained, he said, the society could become lifeless.

At present there are twenty-six ordinary members, representing some 38,000 European physicists, 2,325 individual ordinary members and twenty-six associate members. The rate of recruitment has, however, been slower than expected; the targets for 1972 are an individual ordinary membership of 2,800 and an associate membership at least forty more than at present. But the Wiesbaden conference, which had

1,400 participants, and a concomitant exhibition of instruments, may well have swelled the membership.

Dr L. Cohen, treasurer of the EPS and secretary of the British Institute of Physics, said that it is difficult "to know from year to year where the society stands financially". The EPS was launched in 1968 with several donations and loans, particularly from the



Professor H. B. G. Casimir, president of the European Physical Society.

Battelle Institute, Geneva, and by the beginning of 1971 the outstanding debt amounted to SF 100,000 (about £10,000), which it is planned should be paid off by the end of 1975. 1971 saw a surplus of SF 73,000—largely attributable to a generous single donation—but the projection for 1972, said Dr Cohen, is "that the society might not meet its com-

mitments completely", although it is hoped that a surplus from the Wiesbaden conference will help matters. Dr Cohen said that the situation in 1973 would depend particularly on whether further donations are received, whether the number of associate members (who pay a minimum of SF 1,000 a year) can be increased, and whether the society's house journal *Europhysics News* is to be expanded.

The last possibility was aired by Professor N. Kurti, University of Oxford, who visualized the time when *Europhysics News* would be a much enlarged publication to which would be attached, in the form of brief news bulletins, what are now the house journals of the national societies. Should, in fact, the national societies simply be branches of the EPS?

Naturally enough, many members had their own recipes for solving the financial problems. Several suggestions of a built-in allowance for inflation were made, and it was also proposed that the fee for most individual ordinary members should be increased from its present level of SF 18 a year, or that a fee structure should be set up. It was, however, pointed out that any attempt to allow automatically for inflation in the fees paid to the EPS by national societies themselves could have serious repercussions.

One of the difficulties for the EPS seems to be that any proposed increase in fees that is unlikely to be effective until 1974—the society has legislated for inflexibility by requiring that the council should have six months' notice of such changes.

RESEARCH ASSOCIATIONS

A Difficult Year

IN spite of difficulties caused by heavy spending in order to explore new business opportunities, Sira reports that it has held its own commercially during the past year.

The research association's annual report, published last week, reveals that the grant from the Department of Trade and Industry again decreased in 1971–72 by £14,300 to £212,900—in accordance with the government policy to encourage the research associations to become commercially viable. But this was partly offset by the receipt of more money from royalties, government contracts and contract work from non-member companies. In all, Sira's income from these sources was £38,200

more than during 1970–71.

The report shows that there was no corresponding increase in income in subscriptions from Sira's 135 member companies and the association's turnover decreased by more than £40,000. But Dr Sydney Jones, chairman of Sira, points out in the annual report that a great deal of money was spent to encourage new business which did not materialize until too late in the year to be reflected in the financial statement.

Sira is already thinking in European terms and during 1971–72 it won contracts for equipment or service in Germany and Sweden as well as Japan. The director, Mr S. S. Carlisle, together with members of his staff, also visited companies in Germany, the Netherlands and Switzerland in search of business, and Sira was represented at a DTI exhibition in Germany.

SYSTEMS ANALYSIS

Going International

AN International Institute of Applied Systems Analysis is to be established near Vienna to study the problems of modern civilization. The brainchild of President Lyndon Johnson, the institute is the result of five years work by an international committee under Lord Zuckerman, and has been founded by twelve scientific institutions including the Royal Society, the National Academy of Science and the Soviet Academy of Sciences. It is expected to start work next year at the Palace of Laxenburg near Vienna with a budget to start with of \$3.5 million a year, \$1 million each being provided by the United States and the Soviet Union and the balance by national governments through the other ten national institutions. Britain's contribution will amount to \$150,000. The institute is to be non-governmental and will carry out research in new methods of systems analysis, operational research, management techniques and cybernetics with a view to applying them to the problems that confront society.

Speaking at the first plenary meeting of the institute last week, Mr Michael Noble, Minister of State for Trade and Industry, said that "the age of the computer model is now with us and, from the heated debates about such models, as applied recently to the environment, it is evident that the institute is being born at an auspicious moment when there is as evident a need for a great deal of sound scientific research in the methodology and application of systems analysis".

The first chairman of the council's institute is to be Dr Jermen Gvishiani of the Soviet Academy of Sciences and Dr Howard Raiffa of Harvard University is to be the first director. A permanent staff of between 50 and 100 is to be stationed in Austria, and Sir Kingsley Dunham, chairman of the eighteen-man British National Committee which has been appointed to advise the Royal Society on the conduct of its relations with the institute, said this week that it is hoped that the best brains in the world will be drawn to the institute as visiting consultants.

The institute is to consider projects falling within four chief categories — environmental systems, health and care systems, municipal services systems and large engineering design systems. Although details of the first projects will not be available for two or three months, the Americans are believed to favour an early study of energy resources and demands, coupled with a study of likely new sources and technologies.

Hard-hitting reports on subjects as fundamental to government as those the

institute intends to cover could well be highly sensitive politically, but it is not yet clear how free from political pressure the institute will be. Sir Kingsley said this week that there is no provision in the institute's charter for restrictions on publication, and certainly all the scientists involved hope that publication will be unrestricted, but he added that details of the institute's freedom to publish have not yet been worked out.

The twelve founder institutions of the IIASA are the Soviet Academy of Sciences, the Committee for the International Institute of Applied Systems Analysis (Canada), the Committee for the IIASA of Czechoslovakia, the French Association for the Development of Systems Analysis, the German Academy of Sciences (GDR), the Japan Committee for the IIASA, the Max Planck Society for the Advancement of Sciences (West Germany), the National Centre for Cybernetics and Computer Techniques (Bulgaria), the US National Academy of Science, the National Research Council of Italy, the Polish Academy of Sciences and the Royal Society of London.

RESEARCH COUNCILS

NERC Reports

LONDON may eventually be warned of impending floods by means of an early warning station off the coast of Scotland. The Institute of Coastal Oceanography and Tides has identified a site between 20 and 40 miles east of Aberdeen as the best location for trials of a prototype data buoy which will shortly be available for testing. The objective is to measure offshore sea levels in order to provide early warnings of storm surges in the North Sea. The proposed station, which will not be a practicable proposition for some years yet, should help establish a surge forecasting system for the southern North Sea and Thames estuary.

The details of the scheme are reported in the Natural Environment Research Council's annual report, published last week (HMSO, £1.20). The report also reveals that the long-term downward trend in levels of zooplankton in the North Sea and North Atlantic have continued. Plankton numbers have been recorded since 1948, and the 1970 figures show a general decline in phytoplankton numbers, although in the English Channel and the northern part of the Irish Sea stocks have remained constant.

Dr R. S. Glover, director of the Institute for Marine Environmental Research which is responsible for monitoring plankton, states that the decline has been attributed to pollution but adds that there is no evidence for this assertion. To remedy the situation, the institute plans to record both physical and chemical factors that are known to

affect animals and plants as well as the plankton population.

NERC is also running studies on the site of Maplin airport to discover the effects of London's third airport on wildlife when it opens in 1981. The report says that the site is one of "international scientific importance" and adds that "there will be a need to protect alternative sites for wildlife conservation" as the airport will severely affect the marshes and mudflats near Foulness.

The report lists the council's work in some detail, and provides details of its expenditure, but the council's comments on the current reorganization of government research and development are now of interest to historians only. The report went to press before the white paper was published in July, and whereas the council's evidence to the Select Committee on Science and Technology is included, its comments are restricted to Lord Rothschild's proposals rather than to Lord Jellicoe's decisions. The report does state that "we believe that there should be a closer partnership between the executive departments . . . and the research councils than there has been", and concedes that "in the future an increasing task will be to carry out applied research commissioned by the executive departments". But the council's only comment on the white paper as such is a pious hope that it will have created an environment in which the council can continue its work and "complement the work of the executive departments in a spirit of mutual trust and acknowledgment by them and us of our respective functions . . .".

In the course of the year, the Insect Pathology Unit became a component part of the council with the title Unit of Invertebrate Virology, and the Institute of Marine Biochemistry also joined the council. NERC's expenditure rose from £13.9 million in 1970 to £16.4 million in 1971, and the council's need for computing facilities, discussed at length in last year's report, has been met by the Science Research Council, which has provided facilities at its Atlas and Rutherford laboratories. The Institute of Geological Sciences and the Nature Conservancy remained the biggest spenders among the council's thirteen establishments, accounting for £4.0 million and £2.2 million respectively. The council also financed 679 research studentships in 1971-72 compared with 633 in the previous year. Provisional figures for this year are 732. Expenditure on research grants rose from £0.97 million in 1970-71 to £1.1 million.

SOUTH AFRICA

University Agriculture

from a Correspondent

THE incorporation of South African departments of agriculture into the

universities, as recommended by a Cabinet committee under the chairmanship of Dr C. M. van der M. Brink, is causing some anxiety and upheaval.

Traditionally, South African university faculties of agriculture have been supported by the Department of Agriculture Technical Services, but other university departments have been financed by the Department of National Education. But Dr Brink's committee has now recommended that all the agriculture faculties in South African universities — those at the universities of Pretoria, Orange Free State, Natal and Stellenbosch—be fully incorporated into the universities with which they have been linked.

Dr Brink, who is now President of the South African Council for Scientific and Industrial Research, also recommended that there should only be six chairs of agriculture in each faculty—there are at present between 13 and 20 at each of the four universities.

The committee's recommendations have now been accepted by the Cabinet and all faculties of agriculture have to be incorporated into the university structure by April 1, 1973. The details of the incorporation are being left to the universities but there is an understanding that any staff not supported by the universities will continue to be financed by the Department of Agriculture Technical Services.

The incorporation of the agriculture departments into the university system is also complicated by a review of university finances now taking place. The van Wyk De Vries commission has been sitting since 1969, but so far there are no signs of its recommendations.

Before any major decisions are taken on the future of the departments of agriculture, it is important to know how students are to be subsidized in future. Agriculture departments have attracted only small numbers of students in recent years so that there is a low staff-student ratio. Thus the cost of training students is relatively high, between R1,600 and R3,900 each year. (The highest cost in other fields is R1,100 a year for dental students.)

The Department of National Education is unlikely to support agricultural education at this cost, whence the pressure to reduce the number of departments. Some universities hope to retain all or nearly all of their departments, but this is probably wishful thinking. It is even possible that the Department of National Education will not be able to finance even the six departments recommended by Dr Brink's committee.

Efforts to avoid the inevitable by transferring some of the agriculture departments to other faculties are unlikely to succeed, as this will merely transfer the financial burden to another

faculty probably equally short of funds.

With the April 1 deadline approaching, the picture becomes increasingly confused. Some much-needed light can be thrown on the issues if the van Wyk De Vries commission reports soon.

SOVIET SCIENCE

Joint Mission

from our Soviet Correspondent

THE announcement last week of a four-day joint Apollo-Soyuz space mission in 1975, to be made by Cosmonaut Vladimir Shatalov (veteran of the Soyuz-8 and Soyuz-12 missions), highlights considerable background work which has been taking place in the Soviet Union and the United States since the proposal for a joint mission was first envisaged. The flight plan announced by Major Shatalov is essentially that described by Academician B. Petrov in *Pravda* (August 2, 1972). The flight will take place "in the second half of 1975". The Soyuz craft, with a two-man crew, will be launched first. The Apollo craft with a three-man crew will be launched some 7.5 hours later, although contingency arrangements will permit the Apollo launch to be deferred for up to 48 hours if necessary. Apollo will orbit for about 24 hours before docking with Soyuz. After docking, the joint craft will be operated as a single unit, the two crews working together on scientific experiments for two or three days. Afterwards, each craft will return separately, Soyuz to make a "dry" landing within the Soviet Union and Apollo to splash down in the Pacific.

According to Academician Petrov, work is already in progress on the mechanics of the docking and on standardizing the atmosphere for the joint spacecraft. Soviet spacecraft use air, at normal pressure, whereas the Apollo missions have so far used pure oxygen at reduced pressure. Soviet specialists are hoping that the Americans will consider changing their system. If the Americans insist on pure oxygen, however, an additional airlock will have to be included between the two craft.

In addition to the technical difficulties of docking, special attention is already being given in the Soviet Union to the problems of communication. Petrov's suggestion is that each crew should be thoroughly schooled in the language of the other, with considerable practice to obtain rapid and accurate response to verbal commands. It is interesting, however, that this discussion of the working language suggests a greater emphasis on manual control and less reliance on automation than has been usual in Soviet manned missions to date.

Little has been said so far about

psychological problems—indeed, for a mission of a few days' duration, these may not be significant. If Major Shatalov's prediction of a joint US-Soviet manned mission to Mars by the end of the century reaches the planning stage, however, these factors will have to be considered. The Soviet Union has already done a considerable amount of work on the psychological stresses of simulated deep space flight. Some years ago they claimed that it is unwise to allow crews to play chess or other games of intellectual skill, because these tended to result in disputes, ill-feeling and an inability to cooperate. (Recreations of a less exacting type, where "defeat" would not be felt as a personal failure, were recommended.) Evidently the joint Mars mission is unlikely to involve a repeat of the recent Spassky-Fischer match.

ARCHITECTURAL ASSOCIATION

Thriving School

THRIVING on adversity, the Architectural Association's school has not only survived the decision in July by Mrs Margaret Thatcher, Secretary of State for Education and Science, that local education authorities need no longer pay the school's fees of £580 a year, but has expanded in the process.

Mrs Thatcher's decision meant that 128 students who had places at the school for the current year and who were eligible for local authority grants were no longer sure that these would be paid, but in fact 100 of them have received total or partial grants for fees and only sixteen have been refused; twelve cases are still pending.

The problem arose because it only costs a local education authority between £90 and £180 in fees to send a student to an architectural school attached to a university or polytechnic, but it costs £580 to send a student to the Architectural Association's school. The discrepancy arises because the association is an independent institution, receiving no grant aid, and therefore has to charge a realistic fee. Some local education authorities objected to paying the extra amount, and Mrs Thatcher's decision in fact freed them from their obligation to do so (see *Nature*, 238, 241; 1972). But it now transpires that most of the sixty local education authorities involved have in fact paid up.

Further, the school has expanded from 465 students last year to 619 students for the current session—60 per cent of them British and the remainder foreign nationals.

But the local authorities have yet to agree to support students for the next academic year.

NEW WORLD

Bridges for the Domestic Technology Gap

by our Washington Correspondent

PLANS now being devised in Washington for bringing science and technology to bear on problems such as pollution control, health care and urban renewal have an important factor in common—they deal with issues traditionally the concern of state and local governments. But there are increasing complaints from outside Washington that state and local groups have little or no influence on federal science policy, and that the machinery for transferring technology from federal agencies to the states and localities is inadequate (see *Nature*, **237**, 479; 1972). Last week, these complaints were finally formulated as a series of explicit resolutions drafted by a committee appointed at a conference on this subject in the summer.

The resolutions are printed in an elegant and glossy document whose title, *Action Now**, sums up the message. They are directed at three chief goals—the establishment of state and local representation in the corridors of power in Washington, the strengthening of science policy at state and local levels and the forging of new links between the three levels of government, industry and the universities. Many of the proposals are not new, but most of them could be carried out without much delay and without a great amount of upheaval.

The most persistent theme that ran through the conference and which crops up in the resolutions is the desire for a state and local voice in federal policy making. One recommendation is that there should be established by the White House an Intergovernmental Council for Applied Science and Technology representing federal, state and local governments as well as industrial and academic scientists. Similar representation, the committee suggests, should be included on the policy and advisory bodies of the chief federal agencies concerned with science and technology, on the President's Science Advisory Committee and on the National Science Board. Moreover, to ensure that adequate links are forged between the three layers of government, a senior official should be designated in each federal agency to oversee intergovernmental science and technology.

The idea behind these suggestions is that since most of the new directions of policy in science and technology involve problems such as pollution, where regional disparities are great and which

require action at state and local level, there should be adequate input at the planning stage from those whose job it is to make the policies work. But there is also a strong feeling running through the resolutions that the vast expenditures by the federal government on defence and space research during the past two decades could also bear fruit in applications at the state and local level. Representation on the planning and advisory bodies in Washington may help to transfer some of this technology to the states and localities, but the committee has other ideas for oiling the cogs of the technology transfer machinery.

Thus the committee suggests that federal laboratories should provide consultative and project management assistance to states and localities in applying science and technology to public services. The money for such linkages should come from the National Science Foundation or the Department of Commerce, possibly from the New Technology Incentives Programme now being run by NSF and the National Bureau of Standards. Another idea is that the federal government should provide some money for demonstration programmes for applied research on problems of state and local concern. The suggestion is that such money would be allocated by a board made up of members of state and local government, industry and the universities, and the committee believes that five states should initially take part.

Although, by implication, the committee accuses the federal government of neglecting the task of transferring technology to state and local level, it does not suggest that Washington politicians and bureaucrats are entirely unaware of the problem. Indeed, President Nixon explicitly mentioned the need for forging new links between the three layers of government in his message to Congress on Science and Technology in March, Senator Edward M. Kennedy's National Science Policy and Priorities Act addresses many of the problems involved at the state and local level and the Office of Science and Technology and the National Science Foundation are also trying to bridge the gap. In fact, the domestic technology gap is at least partly the fault of the state and local governments themselves—many state administrations and nearly all state legislatures lack effective science policy advisory machinery, and they are only now becoming aware of their key role in the national science policy network.

Consequently, the committee asks for federal assistance in the establishment of

full-time advisers and advisory groups to state governors as well as technical and analytical staff assistance to legislators. And the committee would also like to see 5,000 additional scientists and engineers in state and local government agencies within three years as well as a regular interchange of scientific personnel between levels of government, industry and the universities.

HUMAN EXPERIMENTATION

Kennedy Tries Again

by our Washington Correspondent

SENATOR EDWARD M. KENNEDY is continuing his attempt to establish federal guidelines for experiments involving human subjects. In August, when the Military Procurement Authorizations Bill came up for debate in the Senate, he attached an amendment which would have prevented federal funds from being used for experiments on human subjects unless they were fully informed of the possible physical and

Over the Hurdles

by our Washington Correspondent

CONGRESS has tied up the few remaining loose ends in the legislation designed to establish an Office of Technology Assessment and has sent the measure to President Nixon for his signature. Although President Nixon has been vetoing all sorts of legislation recently, it is unlikely that he will tread on Congress's toes by refusing to approve a bill that relates only to the legislative branch of the federal government.

Final action on the measure came last week when the House of Representatives agreed to the report of the conference committee set up to iron out the differences between the versions of the bill passed by the House of Representatives and by the Senate. The committee simply dotted a few i's and crossed a few t's in the Senate bill (see *Nature*, **239**, 186; 1972), and its report was accepted without dissent. The office will probably begin its work of contracting out studies of the implications of legislation dealing with technological matters early next year. In the meantime, a suitable director must be found, and that will be no easy task.

*Available from Pennsylvania Office of Science and Technology, Department of Commerce, Room 400, South Office Building, Harrisburg, Pa 17120.

mental effects involved. But the amendment was deleted last month by a conference committee because the House conferees had no time to explore the ramifications of the measure. Last week, however, Senator Kennedy attached a more limited version of the amendment to the Department of Defense Appropriations bill.

The new amendment simply states that "none of the funds appropriated by this Act shall be available for any research involving un-informed or involuntary human beings as experimental subjects". The amendment applies only to the Department of Defense, unlike the original amendment which would have applied to all research pro-

grammes supported by federal funds, and it is therefore less likely to meet strong opposition in the conference committee. As for its effect, it will force the Department of Defense to review its research programmes and draw up fresh guidelines for experiments involving human subjects.

In the same area, a bill designed to set up a commission on the medical, legal and social implications of advances in biomedical research, which was passed by the Senate in December last year (see *Nature*, 236, 344; 1971), has died in the backlog of legislation awaiting action before Congress adjourns. It has not been reported out of the House Commerce Committee.

Controlling the Controllers

by our Washington Correspondent

ALLEGATIONS that the Department of Defense has been tinkering with the weather over Vietnam have given the science of weather modification a bad name. But last week a high level advisory committee recommended that the United States research and development programme into weather modification and control should be expanded, and that a lead agency should be designated to provide a semblance of order for federally supported efforts to control the climate. At the same time, however, the committee has urged the United States to eschew all military uses of weather modification and to conduct research as far as possible on an international basis.

The recommendations were made by the newly formed National Advisory Committee on Oceans and Atmosphere, set up by an act of Congress under the chairmanship of Dr William A. Nierenberg, Director of the Scripps Institution of Oceanography. The basis for the committee's recommendations is its belief that "we are on the threshold of a new era of environmental control"—under limited conditions, rainfall can be increased or decreased, snowpack in the mountains can similarly be modified, cold fogs can be cleared, there are promising methods of suppressing hail and there has been progress in attempts to diminish the force of hurricanes. There is also an increasing body of evidence that man inadvertently modifies the climate through pollutants and urbanization. The committee is, however, equally quick to point out that the potential risks from weather modification are great and now need to be addressed.

Expenditure on weather modification experiments by the federal government has increased steadily during the past few years, from \$16 million in 1971 to about \$25 million in the present finan-

cial year. But the committee believes that the "projects have characteristically been inadequately coordinated, underfunded through fragmentation and often not backed by basic research and undertaken with obsolete equipment". Part of the reason for this sorry state of affairs is that no fewer than seven federal agencies have a finger in the pie, and the chief coordinator of the programmes is a relatively low powered subcommittee of the Federal Committee for Science and Technology.

The committee does concede, however, that the establishment in 1970 of the National Oceanic and Atmospheric Administration (NOAA) in the Department of Commerce, and its subsequent responsibility for monitoring the federal efforts in weather modification, has helped but that "what is lacking is a central focus for the overall effort . . . the present fragmented approach is moving the country ahead in weather modification in an erratic fashion".

The science of weather modification was born in 1946 when Vincent Schaefer and Irving Langmuir conducted their first cloud seeding experiment by dropping pellets of carbon dioxide from an aircraft into a cloud composed of water droplets at below freezing temperature. The dramatic success of this experiment quickly led to a range of weather modification programmes by the federal government, and a number of commercial entrepreneurs also got into the act so that by the late 1950s about 10 per cent of the land area of the United States was under cloud seeding experiments. One problem is that no single agency has been able to regulate all these experiments (even now cloud seeders are not required to report to NOAA before they conduct their experiments) and the committee gives some examples of the chaos which has resulted from this lack of regulation. It is frequently not known whether a

cloud seeding programme is affected by similar experiments nearby. The committee cites a case, for example, in which the National Science Foundation reported that two of its major weather modification projects were seriously compromised by unregulated cloud seeding in the vicinity. In one of the cases an investment of a quarter of a million dollars went to waste.

Apart from asking for a lead agency to plan and regulate weather modification programmes, the committee calls for legislation to define the rights and responsibilities of citizens, the states and the federal government in this area. More basic research in cloud physics is also required, the committee recommends, and it asks that research and development of the technology to mitigate the effects of hurricanes should be accelerated. NOAA's hurricane modification project (Project Stormfury) might be better moved from the Atlantic to the Pacific—a suggestion which NOAA already has in mind but which it has had to defer because of lack of suitable aircraft. Finally the committee recommends that a major federal cloud seeding project should be conducted in the northern Great Plains area of the United States. In this region rainfall is scanty and sporadic and farmers have to trap a portion of one year's rainfall to support agriculture in the next year.

Secretary of Commerce Peter G. Peterson has already welcomed most of the committee's recommendations, but he has expressed some reservations about establishing a focus for the federal government weather modification programme in a single federal agency. He has pointed out that weather modification technology should remain available to all agencies and has suggested that it would be unwise to divorce the research from the agency with the responsibility for applying it. He has also accepted the recommendation for a Great Plains project; plans are already being drawn up.

Short Note

Widespread PCBs

A study conducted by the US Geological survey has found polychlorinated biphenyls in "an unexpectedly large number of sampling points in streams, lakes and reservoirs". Detectable levels of the chemical were found in 17 out of 39 states, including remote areas. In May this year, the Environmental Protection Agency recommended an upper limit of 0.1 microgram per litre in river and lake water, but the USGS survey turned up levels between 0.1 and 4.0 micrograms per litre. The FDA has set a limit of 5 mg per kg in food.

NEWS AND VIEWS

Evolution of Elephants and Suids in East Africa

RECENT and ongoing excavations at Pleistocene and earlier sites along the eastern shores of Lake Rudolf in northern Kenya by Richard Leakey and his colleagues have yielded more early hominids than found at any other fossil locality in east Africa (R. E. F. Leakey, *Nature*, **231**, 241; 1971 and **237**, 246; 1972). As the collections increased it became apparent that here were the remains of two types of hominid. A robust australopithecine, reminiscent of some found at Olduvai Gorge, Tanzania, appears to have lived alongside a much more advanced hominid, although it presumably occupied another ecological niche.

To establish that more than one hominid type coexisted for any length of time—long enough to evolve as distinct groups—demands accurate mapping and relative dating of the horizons in which the hominids are found. It is only in east Africa that there is enough fossil evidence to lend possible support to this model. For not only is there a sufficiency of early hominids of more than one kind but they occur at more than one site, at more than one time horizon and associated with the remains of an abundant mammal fauna. The discovery of these early hominids has focused attention on the problem of Plio-Pleistocene correlation and on the necessity for establishing evolutionary sequences for hominids and other vertebrates.

Traditionally, the rare occurrences of early hominids in Pleistocene deposits have been dated, relatively, from the fauna found associated with them. Special attention was paid to new and rapidly evolving forms, such as the elephant. At one time all the European early hominids had been dated in this way. It was realized, however, that long-range correlations, as between continents, were not advisable. Differential rates of migration and climatic factors had too great an influence on the faunas. With improved collecting techniques it became apparent that faunal barriers exist even regionally and can affect the distribution of animals in nearby sites. This growing awareness of the obvious errors in attempting correlations based on similar faunal assemblages has latterly made stratigraphers at best dubious of such a dating method.

Many palaeontologists, including the palaeoanthropologists, turned to the more absolute methods of dating, in particular to potassium-argon radiometric sampling. This has been of immense importance in establishing sequences at, for example, Olduvai Gorge. Similarly, dating of volcanic tuffs in progress at the East Rudolf sites will, it is hoped, provide an absolute chronology for the area. Already the dating of one tuff (KBS) to 2.6 m.y. indicates that the deposits are very early Pleistocene in age and extend into the Pliocene. Radiometric techniques can usually be applied reliably only to primary volcanic rocks, which themselves seldom contain fossils. Thus radiometric dates from a sequence of basalts or tuffs offer a series of bracketing dates for the intervening sediments and their included fossils. These intervening deposits can represent a very long time during which there can be considerable changes in the fauna of the region, both through *in situ* evolution and migration. For some time there has been a need for a means of filling out and "calibrating" the

radiometric dates; that is, a means of checking their reliability against other dating criteria.

Elephants and suids were among the mammalian groups which during Plio-Pleistocene times were increasing in number and diversity. By meticulous sampling, Maglio (see page 379) has been able to establish trends in the evolution of elephants and suids at East Rudolf based on changes in tooth size. Both the suid and elephant trends show an increase in size and hypsodonty (height) of the molars although the crania remain remarkably constant. These animals are particularly suitable for this technique; their teeth are distinctive and often preserved because of their size and thick enamel. In the elephant three lineages can be traced from mid, or late, Pliocene origins into the Pleistocene, and it is apparent that more than one species coexisted at East Rudolf.

Another rapidly evolving group, that of the suid *Mesochœrus limnetes*, offers a further means of faunal correlation, for the teeth are separable into three size morphs, associated with the three lithological members of the East Rudolf formations. Whether these represent three grades in a lineage or three ecological types further reflected in the different lithologies is irrelevant. To date, they offer the best means of relative correlation at East Rudolf.

Maglio's earlier attempts to correlate between sites are replaced here by a more cautious attitude. It seems that sequences should be established for a given area before attempting longer-range correlation with sequences elsewhere. Although the same species of *Mesochœrus limnetes* is known to occur in the Shungura Formation of the lower Omo Valley to the north of Lake Rudolf and at Olduvai Gorge to the south, Maglio recognizes that at this stage it is more meaningful to restrict comparison to material from the Rudolf area alone. Such correlations as he does attempt are of little value because the method is a long way from being empirical.

Whether hominids, always comparatively rare, were evolving rapidly at this time is impossible to say until more have been found. It seems from published mandible size measurements of the highly variable australopithecines at Koobi Fora and Ileret (R. E. F. Leakey, *Nature*, **237**, 246; 1972) that they hardly show any such trend. Maglio stresses that as a relative dating technique this method is dependent upon the establishment of trends detected in faunal assemblages. Single teeth, or small samples, can be very misleading.

Now that the idea of diversity among the hominids is becoming generally accepted, it is difficult to understand quite why the single species concept for human evolution hung on for so long among palaeoanthropologists. Man is unique in many respects but in his evolution is likely to have followed the pattern of many other groups; that of diversification, adapting to the available ecological niches. That he did this, not once but many times, seems equally probable. Each time the more successful have survived while, with competition and changing conditions, the less adaptable gave up the struggle.—From a Correspondent.

Hydra as a Model Organism

MANY phenomena occurring during the development of multicellular organisms imply intercellular communication. For example the ability to regulate—to produce a standard form independent of size—implies that cells must know their relative position within an embryo. If the two blastomeres of a frog embryo are separated after its first division each will regulate to produce a normal, but small, embryo. Many theories for the mechanism of signalling in embryos have been produced; the oldest, and simplest, is that there is a concentration gradient of a “morphogen” from the animal to vegetal poles, and that cells can measure their ambient concentration and then behave according to their position in the gradient. The production of a stable gradient implies that there is a source of the morphogen at one pole of the embryo and a sink at the other. This kind of model has been used, for example, to explain the production of patterns in the insect integument.

A radically different class of model uses a rapidly propagated signal to supply information to embryonic cells. Whereas such a system might have many advantages, the only example of its use in a real organism is in the signal controlling aggregation in some cellular slime moulds. It is questionable whether one can safely draw analogies between the development of slime mould and that of more complex organisms. On the other hand, it is clearly important to understand the processes controlling development in simple organisms, or in circumscribed situations in metazoan embryos. For this reason many simple “model” systems are popular amongst developmental biologists. Two articles in a recent issue of *Nature New Biology* are concerned with hydra, which already has a distinguished career as a model organism.

Hydra can regenerate and regulate. If the head of a hydra is removed a new head regenerates at the anterior cut surface. This regeneration does not require cell division, but stems from a reorganization of the tissues of the hydra. Further, the presence of an extra head nearby can inhibit head regeneration at a cut surface. The implication is that a head acts as a source of some substance that actively inhibits head formation, and possibly also supplies “positional information” to cells within the hydra. When a head is removed the gradient of inhibitor relaxes and, it is postulated, when the concentration of inhibitor has fallen below a threshold value, which is a function of axial position, new head formation is initiated. If these postulates, due to Wolpert and his colleagues, are correct, then hydra does indeed provide an ideal experimental system for investigating signalling during the control of a developmental process.

Wolpert, Clarke and Hornbruch (*Nature New Biology*, **239**, 101; 1972) have investigated the rate of propagation of the inhibitory signal. Their basic experiment involves the determination of how long an extra head must be grafted into the axis of a hydra in order to prevent head regeneration when the hydra's original head is removed. In this way one can measure the time required for a head to set up its own inhibitory field. By varying the position on the axis at which the extra head is grafted it is also possible to find the time required for inhibition

as a function of distance. At first sight it would seem that this time should increase as the square of the axial distance if inhibition depends on the diffusion of a substance from a head region. A grafted head is, however, supplying inhibitor to a field which already contains an original inhibitor gradient, so the relationship is more complicated.

The results of Wolpert *et al.* show that the times for signal transmission get quite long, and indeed are not consistent with a rapid signal such as an electrical or chemical impulse propagated from cell to cell. They have made reasonable assumptions about the shape and production of the underlying inhibitor gradient and have used these in a computer simulation of the signalling process. The simulation shows, quite successfully, that diffusion of a relatively small molecule, such as a nucleotide, could well account for the propagation of the inhibitory signal.

This is an important result, although one should be careful to avoid reading too much into it. Such simulation involves enough free parameters to make it difficult to do more than show a consistency between the model and the experimental data. In this case, for example, it would be necessary to determine the chemical nature of the inhibitory morphogen before one could make unequivocal tests of the model. This, of course, is a problem besetting all theoretical interpretations of biological events; biological systems are so complex that it is possible to pick enough variables to fit any model to the facts.

A further capability of hydra is reconstitution of an individual from dissociated cells, as Gierer *et al.* show (*Nature New Biology*, **239**, 98; 1972). Again, this provides an important model system for examining the development of polarity and positional information, and the subsequent control of cell movement and differentiation. In their experiments, Gierer *et al.* find that dissociation of hydra, by mechanical disruption, into single cells and small groups of cells can be followed by re-aggregation and regeneration. They show that the composition of groups of cells or cellular constituents determines polarity within the regenerating organism, defining its axis. Polarity does not depend on the orientation of single cells. Again, a mechanism for setting up positional information to control development is probably involved. Furthermore, the earliest stages of reorganization do not require cell division, although a minimal proportion of epithelial cells is needed. Cell division does appear to be necessary for some subsequent differentiation. The system is therefore useful for investigating the control of differentiation as well as for determining how cells know and remember their position within a hydra axis. As Gierer *et al.* show that even dissociated cells show some memory of their original position, it should be possible to find what kinds of biochemical treatment before reaggregation can disrupt this memory. Presumably the relevant biochemical mechanism is related to the mechanism responsible for the inhibitory signal, emanating from the head region, investigated by Wolpert.—From a Correspondent.

NUCLEIC ACIDS

Nucleotide Rigidityby our Biomolecular Structure
Correspondent

THE importance and interest of the crystal structure of the dinucleoside uridylyl 3',5'-adenosine phosphate (UpA) was noted in these columns when Sussman *et al.* gave their preliminary account of the analysis (*Nature New Biology*, **233**, 90; 1971). Since then an independent determination of that structure has been reported by Sundaralingam and his co-workers (*Science*, **174**, 1020; 1971), along with detailed accounts of the analysis by both groups of workers (Sussman *et al.*, *J. Mol. Biol.*, **66**, 403; 1972; and Rubin *et al.*, *Biochemistry*, **11**, 3112; 1972). Apart from the degree of independence of the two analyses, which is apparently a matter of some dispute (*Science*, **177**, 294; 1972), the two accounts have a considerable interest from the point of view of the evolution (some might say embroidery) of our ideas of nucleic acid stereochemistry.

Sussman *et al.* made the point that all four nucleosides in the structure (there are two dinucleosides per asymmetric unit in the crystal) have, first, the *anti* conformation about the sugar base link, second, the 3'-endo 2'-exo sugar pucker, and third, what might be a C-H...O hydrogen bond between the 5' O and a ring carbon of the base to which the sugar is attached. They cautiously concluded that it may well be reasonable in model building studies of polynucleotides to regard nucleosides as roughly rigid structures. Sundaralingam and colleagues note essentially the same stereochemical features but conclude somewhat more triumphantly "the concept of a rigid nucleotide unit developed here and elsewhere (Sundaralingam, in *Conformations of Biological Molecules and Polymers*, Bergmann, E., and Pullman, B., eds., Jerusalem, Israel Academy of Sciences and Humanities) makes a turning point in the history of nucleic acid structural research. This concept, which parallels the development of the rigid peptide unit (Pauling and Corey, 1953), is expected to have far-reaching consequences in understanding conformations of polynucleotides." This statement reminds one that even if the world does seem to be an unappreciative place, writing one's own epitaph requires some care. Perhaps with so many of the riches of molecular biology on offer to crystallographers (or to use the classic phrase "up for grabs") we should not be too sensitive to such trumpeting.

Apart from their style, however, the validity of these conclusions merits a few cautionary remarks. First, it may be that in the search for conformational certainty for polynucleotides the analogy with the peptide group was not a par-

ticularly happy one. The work of Winkler and Dunitz (*J. Mol. Biol.*, **59**, 169; 1971) contains the conclusion that "in the construction of models of polypeptide chains or in fitting such models to electron-density maps of protein crystals, the strictly planar peptide unit thus incorporates restrictions that may be rather easily relaxed in the actual molecule." Even if it is a reasonable first assumption, however, that the amide group is planar, it should be recognized that this group with its resonance character is not at all analogous to the saturated sugar ring. It is true that in single crystal determinations of nucleotides and nucleosides two predominant types of sugar pucker are observed. Within each type, however, the standard deviation of a single torsion angle which can be used to describe the pucker is about 6° corresponding to an expected range of variation in this angle of about 20°. Such variability about both types of sugar pucker can lead to considerable uncertainty in the expected conformation of a polynucleotide chain containing a number of sugars.

In addition to the pucker of the sugar ring, five other torsion angles are required to define the conformation of the sugar phosphate part of each nucleotide within a polynucleotide chain. Although it is true that preferred values for many of these angles are recognized (particularly from the careful surveys of Sundaralingam) it is not clear that they are anything like so well defined as the paper by Sundaralingam *et al.* suggests. In fact Table 9 in this paper which surveys the allowed ranges is, on close examination, not at all convincing, even when what must be a record number of errors in a published table are corrected.

The final cautionary comment on the

rigid nucleotide hypothesis is a general one. What evidence we have suggests that as the crystal structures of more and more complex nucleic acid components are determined we can expect more and more surprises. The history of the observation of *syn* conformations about the sugar base link can be taken to point the way here, and there are already signs that stereochemical "peculiarities" occur more frequently in the structures of larger than smaller molecules—presumably as a consequence of the compromises necessary to satisfy an increasing variety of interactions. It is as well to remember that the biological structures where stereochemical information from structure determinations such as those discussed here is most relevant, such as the loops in tRNA molecules, are very often themselves very complex structures where "peculiarities" may be commonplace.

NUCLEAR MAGNETIC RESONANCE

Josephson Detector

from a Correspondent

A NOVEL approach to the detection of nuclear magnetic resonance has recently been developed by Day (*Phys. Rev. Lett.*, **29**, 540; 1972); the resonant radio frequency (r.f.) excitation is observed by means of a Josephson junction magnetometer (Zimmerman and Silver, *Phys. Rev.*, **141**, 367; 1966) and this new technique will allow broad lines to be measured with considerably lower r.f. field levels than previously. For example, Day has measured the magnetization of the nuclei in LiF at room temperature in a field of 7.47 k oersted using 40 dB less power than is required

Difficulties in Telling QSOs from Blue Stars

SINCE the discovery of QSOs, observational astronomers have had the problem of picking these blue, star-like objects out of sky survey plates which include many genuine blue stars. One of the most useful aids in resolving this difficulty has been the rule of thumb that QSOs usually show a characteristic ultraviolet excess; but this rule breaks down on occasion, and in next Monday's *Nature Physical Science* I. W. A. Browne and N. J. McEwan, of the University of Manchester, discuss the identification of eleven radio sources which are believed to be associated with stellar objects "which although they appear blue on the Palomar Sky Survey Prints, do not show the characteristic ultraviolet excess".

These eleven objects are part of a group of seventeen which were noted in the Parkes 2,700 MHz survey (Wall *et al.*, *Aust. J. Phys. (Astrophys. Suppl.)*, **19**; 1971). All seventeen radio sources

are close to blue stellar objects which have no ultraviolet excess; Browne and McEwan have now shown that more accurate radio positions still result in error boxes which include the blue stellar object in eleven of the seventeen cases. Could this result from a chance superposition of radio sources and stars? The Manchester group think not, and go on to suggest that the proposal made by Bahcall and Sargent (*Astrophys. J. Lett.*, **148**, L65; 1972), that QSOs with redshift greater than 2.3 do not exhibit ultraviolet excess, is supported by the latest observations. Their conclusion is that although two colour (blue and ultraviolet) plates are useful for confirming suspected QSOs, the technique should not be used for rejecting possible identifications. This will strike a gloomy chord for those trying to unravel the secrets of the universe by making number counts of these sources.

for the conventional fast passage method.

Under conditions of adiabatic fast passage the frequency of an r.f. field is changed from below the nuclear resonant frequency to above it at such a rate that the nuclear magnetization is inverted. Thus, considering the equilibrium situation in which the nuclear magnetization is parallel to the applied steady field, H_0 , traversal of the line under conditions of adiabatic fast passage causes the magnetization to rotate from a direction parallel to the steady field to one that is antiparallel. In the "halfway" position the nuclear magnetization is transverse and precesses at the resonant frequency; it can therefore induce a voltage across a coil placed with its axis perpendicular to H_0 that is proportional to the nuclear magnetization. If, however, the resonance line has a width δH which is comparable with the strength of the r.f. field H_1 , the apparent nuclear magnetization is reduced, for all the magnetization is not transverse at the same time. The conventional method of measurement removes this difficulty by increasing the level of H_1 . Day's new method, on the other hand, does not rely on the measurement of the transverse magnetization; instead, the difference in longitudinal magnetization before and after the inversion (namely twice the nuclear magnetization) is observed. Thus smaller r.f. fields may be used. The extremely sensitive method of Josephson junction magnetometry is used to measure the change in the longitudinal magnetization.

Day suggests that the new technique will find application in isotope trace analysis in solids, in geological dating, in thermometry, and in the study of broad nuclear resonance lines in biological molecules.

SV40 TRANSCRIPTION

Hidden Subtleties

from our Cell Biology Correspondent

LIKE a man who has fasted and then guzzled a feast only to suffer acute indigestion, those intent on elucidating the regulation of expression of SV40 and polyoma virus genomes in permissive and non-permissive cells suddenly find themselves accumulating new experimental data faster than they can digest them into a satisfactory hypothesis; they are learning more and more but, for the time being at least, understanding less and less.

Earlier this year Khoury and Martin (*Nature New Biology*, **238**, 4; 1972) and Lindstrom and Dulbecco (*Proc. US Nat. Acad. Sci.*, **69**, 1517; 1972), reported data which indicate that during the lytic cycle of SV40 in monkey cells before the replication of viral DNA

begins, RNA is transcribed off one strand of the SV40 DNA, but late in infection, after DNA replication has started, RNA is transcribed off parts of both SV40 DNA strands. Furthermore the DNA strand transcribed before DNA replication begins is the strand which is transcribed exclusively *in vitro* by *Escherichia coli* RNA polymerase. These observations indicated that the regulation of transcription of SV40 DNA *in vivo* involves a strand switching event.

Subsequently Khoury, Byrne and Martin (*Proc. US Nat. Acad. Sci.*, **69**, 1925; 1972) estimated the extents to which the two SV40 strands are transcribed in permissive and non-permissive cells at various times after infection. In brief they reported that early during the lytic cycle about 35–39 per cent of the minus or early strand is transcribed and that at late times 38–42 per cent of this strand and 60–64 per cent of the complementary plus or late strand is transcribed. Moreover in non-permis-

sive primary mouse embryo cells some 24 h after infection with SV40 the extent and pattern of transcription are almost identical to that in permissive cells late in infection. A third group, Sambrook, Sharp and Keller, which has been investigating these events, has now reported (*J. Mol. Biol.*, **70**, 57; 1972) results of experiments with lytically infected cells which are consonant with those of the two other groups. Sambrook *et al.* estimate that early in the lytic cycle about 30 per cent of the minus or early strand is transcribed whereas late in infection viral RNA is homologous to 30–35 per cent of the early strand and to about 70 per cent of the complementary late or plus DNA strand. Sambrook *et al.* also report that in transformed mouse cells (SV3T3) the viral RNA is homologous to about 50 per cent of the early or minus strand and 15–20 per cent of the late or plus strand. Apparently the pattern of transcription of SV40 DNA differs in SV3T3 cells and abortively infected

Lower Mantle Inhomogeneity

THE existence of inhomogeneities in the lower mantle is either implicit or explicit in several recent suggestions — for example, in Morgan's (*Amer. Assoc. Petrol. Geol. Bull.*, **56**, 203; 1972) postulation of hot spots in the lower mantle, and in Anderson's (*Comments Earth Sci.: Geophys.*, **2**, 93; 1972) inhomogeneous planetary accretion hypothesis which requires refractory nuclei at the base of the solid mantle. There is also a little experimental support for such inhomogeneities. Phinney and Alexander (*J. Geophys. Res.*, **71**, 5959; 1966; and **74**, 4967; 1969), for example, concluded from spectral differences in long period P waves diffracted beneath the Pacific Ocean that an average seismic velocity gradient of 0.2 km s⁻¹ per 100 km was required in the lower mantle.

In next Monday's *Nature Physical Science*, Kanasewich *et al.* report further experimental evidence for a lower mantle inhomogeneity—this time beneath Hawaii—from a study of P wave arrivals at the seismic array VASA in central Alberta. It seems that P waves arriving from earthquakes near the Tonga Islands have anomalous phase velocities with respect to the Jeffreys-Bullen tables and to the Birch Earth model II. At epicentral distances of 84° phase velocities are normal, but at 95° they are as much as 15 per cent higher than expected. By contrast, no such anomalies are observed from other sources beneath the Pacific, South America or Asia even though they are at comparable distances.

Explanations for the anomalies other than that of a lower mantle inhomogeneity are possible but are ruled out by

Kanasewich and his colleagues. For example, inhomogeneities in the source region as the cause of the anomalies are unlikely, partly because the array is very insensitive to the effects of inhomogeneities at this level and partly because phase velocities are obviously not affected by crustal structure in most other source areas. Nor is it likely that the anomalies are due to bumps on the core-mantle interface. What seismic evidence there is suggests that any such bumps cannot be more than a few kilometres high whereas the anomalous phase velocity observed would require a depression of 125 km in the surface of the core.

Kanasewich *et al.* thus favour the view that the anomalies are caused by a laterally and radially inhomogeneous lower mantle region beneath Hawaii. More specifically, the characteristics of the inhomogeneity are a velocity gradient of 0.13 km s⁻¹ per 100 km in the Earth radius range 3,510 to 4,000 km and a high velocity (about 14.7 km s⁻¹) segment between 3,473 and 3,510 km. Lateral limitations (E-W) may be placed on the size of the inhomogeneity by virtue of the fact that shocks from Fiji and from the southern end of the Tonga region give waves with normal phase velocities. In the vertical direction, the data available offer no evidence for an extension of the inhomogeneity above a radius of 4,000 km. On the other hand, such a possibility is not excluded; and thus in this sense Wilson's (*Can. J. Phys.*, **41**, 863; 1963) suggestion that the Hawaiian lavas originate from a mantle source in a near-stagnant convection cell centre is not contradicted.

primary mouse embryo cells but that is not particularly surprising.

The simplest interpretation of all these observations is, of course, that the regulation of expression of SV40 DNA occurs at the level of transcription and involves strand switching after DNA replication begins. Experiments now reported by Aloni (*Proc. US Nat. Acad. Sci.*, **69**, 2404; 1972), however, indicate that the situation is a good deal more subtle than it appeared at first sight. Using short pulses (2 min to 20 min) of ^3H -uridine to label SV40 RNA made at late times in monkey cells, Aloni has shown that both strands of SV40 DNA are extensively transcribed and that subsequently particular sequences in the two complementary RNA transcripts are selectively degraded by RNAase. In other words, at least late in the lytic cycle the regulation of expression of SV40 genes occurs at the post transcriptional level and involves the selective degradation of some SV40 RNA. Aloni, together with Attardi, has, of course, shown that the transcription of HeLa cell mitochondrial DNA is also symmetric and apart from the raising the question of how selective RNA degradation is achieved these two sets of observations raise the possibility that post transcriptional regulation of gene expression may be a more widespread phenomenon that has previously been countenanced.

CONTROLLED FUSION

Tokamaks to Win?

from a Correspondent

RESEARCH on controlled fusion and plasma physics is now conducted on such a scale that there must be one large international conference every year. By agreement the conferences of the European Physical Society alternate with those of the International Atomic Energy Agency and are now almost equally international in character. Certainly the Fifth European Conference held at Grenoble from August 21 to 25 had strong representation, not only from the Soviet Union (which appears in its own right as a European nation) but also from the United States, Japan and elsewhere.

The most frequently used word at the conference was undoubtedly Tokamak. Since the introduction of this axisymmetric toroidal concept for plasma confinement by members of the Kurchatov Institute in Moscow in the early 1960s, it has gradually gained ground against fierce competition from other ideas for magnetic plasma confinement (notably mirrors, high- β pinches and stellarators), and an uninformed observer at the Grenoble conference might well be forgiven for supposing that its victory is secure. Indeed it is

now a hallmark of scientific respectability in a fusion laboratory to possess a Tokamak, and already seven have been (or are being) constructed in Europe, seven in the United States and six in the Soviet Union. This is not, of course, simply the pursuit of fashion: any fusion laboratory wants to have a plasma at something like the temperatures and densities required for a fusion reactor with a lifetime measured in milliseconds, if only to get its feet wet in the new technology involved.

This does not mean, however, that Tokamaks are without problems. In the first place, the plasma pressure confined within a Tokamak has not yet reached the level at which one could hope to design an economic reactor, and it is still unclear whether this is a difficulty of principle or not. In this context one uncertainty has been how small the Kruskal-Shafranov "stability safety factor" q can be, for the maximum attainable pressure theoretically scales as $1/q^2$, and a value $q=3$ would have seriously unfavourable implications. In many Tokamak experiments, for example those reported by Stodiek (Princeton University), a "disruptive instability" is encountered as q is reduced below 3, and one of the interesting new results of the conference was a provisional identification of this as the well known "tearing instability". The Soviet Tokamak group at the Kurchatov Institute have, however, now succeeded in pushing past this instability barrier around $q=2$, and the paper presented by Strelkov gave a convincing demonstration of the possibility of reaching $q=1$.

A second problem in Tokamak research has been that at present they can only operate with a very restricted range

of plasma parameters, and all attempts to raise the density or temperature (both of which need to increase by a further factor of five to reach reactor conditions) have been blocked either by the "disruptive instability" or by the "run-away electron" phenomenon. Consequently much effort has been devoted to the search for new procedures to supplement the basic ohmic plasma heating mechanism in a Tokamak. Of the five methods under consideration, three were shown to be feasible, at least at low heating rates, one (injection of high energy neutral atoms) remains untried but promising, and one has encountered serious, though not necessarily insuperable, difficulties. The Princeton group relies on ion cyclotron heating, and has so far supplied 15 kW, amounting to about 15 per cent of the ohmic heating rate, which raised the ion temperature of a rather cool Tokamak plasma ($T_i=50$ eV) by a factor of two. The Kurchatov group, using electron cyclotron heating, raised the electron temperature from 500 to 2,000 eV in a rather low density plasma ($n_e=10^{12}$ cm $^{-3}$). A group at the Ioffe Institute in Leningrad reported strong absorption of r.f. power by the plasma at the lower hybrid frequency. The one discouraging note was the paper presented by Millar (Culham Laboratory) on the effect of transit time magnetic pumping on a toroidal plasma, which produced negligible heating but a rapid "pump-out" of plasma to the walls.

The outstanding problems facing Tokamak designs are such that it is certainly premature to abandon other toroidal confinement concepts, and it was clear from the conference that important work is still in progress on high- β toroidal pinches and on stellarators.

Methylation of Bovine Rhodopsin

BOVINE rhodopsin can now be added to the growing catalogue of proteins which contain methylated basic amino-acid residues for, as Reporter and Reed report in next Wednesday's issue of *Nature New Biology*, bovine rhodopsin contains monomethyl, dimethyl and possibly trimethyl lysine residues. Furthermore they have found that an uncharacterized protein associated with rhodopsin also contains trimethyl lysine and dimethyl arginine residues.

Reporter and Reed incubated freshly dissected bovine retinas overnight in a medium containing ^3H methyl methionine and subsequently solubilized the rhodopsin and other proteins of the retina with a non-ionic detergent and separated them by gel electrophoresis. The rhodopsin contained most of the ^3H methyl groups incorporated into amino-acids during the incubation period. Aliquots of rhodopsin isolated

from rod outer segments after an overnight incubation with ^3H methyl methionine were then hydrolysed and the hydrolysates were separated by paper electrophoresis. Most of the radioactivity in amino-acids was found to be in methylated lysine residues.

Using standard Moore and Stein columns, Reporter and Reed then analysed methylated monomeric rhodopsin and found that of the ten lysine residues in each monomeric rhodopsin molecule one or two are probably monomethylated and four are probably dimethylated. In addition two of the five histidine residues appear to be trimethylated. As Reporter and Reed point out the methylation of the basic amino-acids of the opsin protein of rhodopsin may confer resistance to enzymatic degradation and it may also facilitate the attachment of the 11-cis retinal chromophore.

The former seek to avoid the plasma pressure limitations inherent in the Tokamak concept either by grossly distorting the cross-section of the toroidal plasma column, producing a belt-shaped plasma, or by programming the magnetic field in time so that a configuration is produced in which the toroidal magnetic field has opposite directions within and outside the plasma, or by adding windings which remove the axial symmetry of the magnetic field but provide stabilizing "shear". The first approach was described by Zwicker, whose device ISAR IV at Garching is now in full operation, and producing quite impressive plasmas, with pressures comparable with the confining magnetic pressure. The latter approaches are exemplified by the HBTX experiment at Culham and the various precursors to the Scyllac experiment at Los Alamos, which were reported by Jahoda. Conventional stellarators are at present rather out of favour, for their confinement properties seem to be, if anything, inferior to those of Tokamaks, and the cost and complexity of their helical windings are much greater. Some interesting work on the experimental confirmation of a theory due to Volosov of the anomalous plasma loss mechanism was reported by a group from Novosibirsk.

The only non-toroidal confinement configuration which is still a serious contender is the mirror machine. The principal problem which this approach has to face is the high rate of loss of plasma through the mirrors due to Coulomb collisions, and the possible further enhancement of this loss due to collective plasma processes. A theory of this enhancement, due to "loss-cone instabilities", was recently given by Callen and Baldwin of Livermore, and Coensgen reported some rather impressive experiments on the 2×2 device at Livermore which strongly suggest that this mechanism does account for the discrepancy which previously existed between the observed loss rate and the Coulomb collision loss rate, and it seems possible that a similar mechanism might explain the discrepancies reported by two mirror groups at Fontenay-aux-Roses.

Finally, there were a few papers on the radically different approach to controlled fusion, in which one heats the plasma extremely quickly and relies upon inertia to prevent it from expanding before the thermonuclear reactions have taken place. Three fast plasma heating procedures have been suggested—a rapid θ -pinch implosion giving a short lived axial field of several Mgauss, a relativistic beam with a high current interacting with a solid target, or a nanosecond giant laser pulse heating and compressing a spherical solid hydrogen target.

PROTEINS

Concanavalin Observed

from our Molecular Biology Correspondent

CONCAVALIN is a name that nowadays elicits Pavlovian salivation in cell biologists and others. It is also a protein, one of the so-called lectins, which derive from plants and possess the property of agglutinating erythrocytes and other cells. They do this by binding to saccharide residues on the cell surface and, in the case of concanavalin A, the interaction with saccharides, which depends itself on the presence of calcium and manganese ions, has been studied in great detail. Not long ago, Hardman and Ainsworth (*Nature New Biology*, **237**, 54; 1972) obtained a difference electron density map between crystals of concanavalin with and without inositol and found that the sugar residue is lodged below the surface of the protein, in a cavity. The polypeptide chain contours around the binding site could be made out, and the side chains making up the cavity were identified. The manganese ion, which is indispensable for binding of the sugar, is remote from the binding site. The difference map also reveals that association with inositol causes small structural changes in the protein. An odd feature is that the binding site for an iodophenyl derivative of another saccharide, D-glucopyranoside, studied

by other workers, does not coincide with that of inositol.

Now Edelman *et al.* (*Proc. US Nat. Acad. Sci.*, **69**, 2580; 1972) describe their structure of concanavalin A at 2 Å resolution, and concur in this curious finding. The protein, which in solution is predominantly a dimer, packs as pairs of dimers in the crystal, with the monomer as an asymmetric unit. The conformation contains a high proportion of antiparallel β -structure, and hardly any α -helix; β -chains extend across the interface between the subunits of the dimer. The binding sites for the manganese and calcium ions are inferred from peaks of electron density that cannot be accounted for by side chains. The manganous ion, it appears, has a more or less octahedral coordination shell, four carboxylate and one imidazole ligand contributed by the protein, the remaining two presumably by water. The calcium coordination is similar, with one backbone carboxyl and four carboxylate ligands. Two of the carboxylates, identified as aspartate side chains, are common to the coordination shells of both metal ions, which leads to a rationalization of the manganese-contingent binding of calcium, in terms of a stabilization of the local geometry by the manganese.

As to the binding site for the iodophenyl-D-glucopyranose, the iodine lies in a deep cavity, and is surrounded

Clustering of Concanavalin A Sites after Proteolysis

THE nature of the changes in the surfaces of cells, induced by transformation by tumour viruses or by exposure to proteolytic enzymes, which results in an increased susceptibility to agglutination by plant lectins such as concanavalin A is currently a matter of some controversy. One school argues that enhanced agglutinability is caused by an increase in the number of lectin binding sites exposed at the cell surface while the other maintains that changes in the topographic distribution of the sites rather than their number are responsible. In next week's *Nature New Biology* Nicolson, who belongs to the latter school of thought, reports further comparative investigations of the distribution of ferritin conjugated concanavalin A molecules bound to the surfaces of mouse 3T3 cells which have been exposed to trypsin or have been left untreated.

Nicolson reports that ferritin conjugated concanavalin A molecules are found in clusters on the surfaces of 3T3 cells exposed to mild digestion by trypsin whereas they are randomly distributed on the surfaces of untreated 3T3 cells; exposure to trypsin also, of course, renders the cells more readily

agglutinable. Both the size and the distribution of the clusters of lectin bound to cells exposed to trypsin resemble those on the surfaces of 3T3 cells transformed by SV40. Moreover, when cells are exposed to extremely dilute trypsin they do not become more readily agglutinable and the ferritin conjugated concanavalin A remains randomly distributed. To show that the clustering of receptor sites is directly involved in agglutination, Nicolson examined thin sections of agglutinated cells and found that the concentration of the tagged lectin was much higher in those regions where the surfaces of two cells were in close apposition than in regions where the cell surfaces were not in contact.

These experiments strongly suggest that cell agglutination caused by polyvalent agglutinins depends at least in part on the clustering of binding sites. Such clustering implies, of course, that membrane components are free to diffuse in the plane of the membrane and presumably clustering is facilitated by mild proteolysis of cell surface. Such digestion might alter the electrostatic properties of the surface as well as the conformation of surface proteins.

by mainly hydrophobic side chains. The heavy atom obscures the rest of the ligand, which, however, is surmised to be oriented towards the surface. A number of side chains, including three serines, may be implicated in the saccharide binding site. In terms of the model of Edelman *et al.* the inositol-binding locus appears to be close to the slot housing the iodine, and too far therefore from the D-glucopyranose site to be identified with it. Edelman *et al.* maintain, because inositol is not, according to them, an inhibitor of the haemagglutination reaction, whereas their D-glucopyranose derivative suppresses both this and binding to polysaccharides, that the inositol binding mode is not functionally relevant. This may be, however, and the structure does not in any case at this stage throw any direct light on the physiological activity of concanavalin. It is generally supposed that the primary feature of its interaction with cells is its ability to cross-link receptor sites, by virtue of its stable dimeric, therefore divalent, structure. Its effect on mitogenesis is surmised to involve in the first place the promotion of cluster formation between the membrane glycoproteins: as it now seems clear that proteins are able to diffuse quite rapidly in the plane of the cell membrane, a bifunctional reagent like concanavalin will be expected to give rise to cross-linked oligomeric or polymeric networks. The possibility also exists of some secondary reaction with the cell surface following binding. Yahara and Edelman recently showed (*ibid.*, 608) that concanavalin inhibits the coalescence of immunoglobulin on lymphocytes under the action of immunoglobulin-directed antibodies. The immunoglobulin-receptor complex is evidently free to diffuse in the membrane, and the anti-immunoglobulin antibody possesses again the ability to induce formation of a network. The structures that the concanavalin generates in the membrane evidently impede the motion of the immunoglobulin-receptor complex, or perhaps trap it by combining with it.

Along the same general lines, Shoham and Sachs (*ibid.*, 2479) have shown that tissue-culture cells in different stages show differences in their response to fluorescein-conjugated concanavalin A. Amongst other effects that are found, transformed cells give a higher yield of fluorescence, and so also do normal cells after limited trypsin treatment. Time effects may be presumed to reflect the operation of a diffusion mechanism. It is not yet clear whether the differences depend on the availability of receptors, or, as seems to be the case for immunoglobulin receptors in erythrocytes, on differences in their capacity to form clusters.

FORENSIC SCIENCE

Nuclear Detectives

from a Correspondent

SOME of the most useful and perhaps surprisingly the least advertised benefits of nuclear technology have come from the application of activation analysis to forensic problems. The scientists and police officers from 30 countries who gathered in Glasgow from September 27–29 for the second International Conference on Forensic Activation Analysis reviewed the achievements (and occasional shortcomings) of the technique in topics as diverse as ballistics, toxicology, attribution of paintings and detection of counterfeit whisky.

Activation analysis, defined as the revelation of atomic composition through the modification of nuclear behaviour, is essentially a chemical technique involving the bombardment of the sample by neutrons (or, sometimes, other particles or radiations) followed by an assay of the induced radioactivity. When access to a nuclear reactor is available, the procedure is relatively simple and, for many elements, extraordinarily sensitive; for example the arsenic content of a one millimetre length of a single hair can readily be measured.

The forensic uses of activation analysis depend mainly on the detection and estimation of trace elements in material gathered from the scene of a crime or from a suspect. During the 1960s it was claimed that an individual could be identified by the trace element content of a hair. Some constituents of hair, such as sodium and zinc, show relatively little variation

among individuals and are therefore not useful for identification. Other elements show considerable variation in concentration over a head, along a single hair, and it also varies according to diet and environment. Though some workers reported otherwise, R. Cornelis (Ghent) declared forthrightly that identification by activation analysis of hair is impossible.

Analysis of non-biological materials is less controversial. In some countries crimes involving shooting are routinely investigated by estimation of antimony and barium present in cartridge primers and on hands and clothing after firing. Study of such deposits around a bullet hole or wound allows the firing distance to be estimated. W. B. Renfro and W. A. Jester (Pennsylvania State University) showed how activation analysis of airborne residues allows the time elapsed since the firing of a shot to be estimated.

E. V. Sayre (Brookhaven National Laboratory) and colleagues from a number of laboratories and galleries in the United States described tests involving neutron bombardment of art work, followed by autoradiography, to reveal otherwise inaccessible details of materials and techniques serving to confirm or correct the attribution.

F. W. Lima (São Paulo) told of studies on counterfeit whisky. The bottles, labels, corks—and even the contents—were not distinguishable chemically from the genuine articles, but the lead foil caps were found, by anomalies in tin and antimony content, to be of local manufacture. The object of the well-planned counterfeiting was to sell Brazilian whisky (of its kind, quite good) as a genuine Scottish product at an inflated price.

Crystallization of Polyethylene

IN next Monday's *Nature Physical Science* evidence is presented to show that there are two distinct processes involved in the crystallization of polyethylene. D. C. Bassett, B. A. Khalifa and B. Turner of the J. J. Thomson Laboratory at the University of Reading report that the two processes dominate at low and high pressures, respectively, and by so doing they dispose of several suggested origins for the effect.

Crystallization of polyethylene at high pressures leads to crystals whose lengths along the chain direction are commensurate with the lengths of molecules. These crystals are known as extended chain crystals and are usually one or two orders of magnitude greater than the crystals obtained at atmospheric pressures.

The two distinct processes show up clearly in the work of Bassett and colleagues and it is shown that the change over from one form to the other occurs

within a temperature range of only 5° C when a sample of polyethylene is crystallized at a pressure of 2.87 kbar, which is in between the high and low pressure limits.

Another feature of the work of the Reading team is that it is shown that the pressure at which one form of polyethylene changes into another form depends on the molecular weight of the polymer. But the unexpected result of this work is that the lower the molecular weight the higher the pressure required for the change to occur. Thus it turns out that it is easier to crystallize longer molecules into the very long chain-extended crystals than it is to crystallize the shorter ones.

This experimental result is the exact opposite of the prediction of T. Kawai, whose explanation of the phenomena requires that the lower the molecule weight the greater should be the tendency to form longer crystals.

OCEANOGRAPHY

Challenger Centenary

from a Correspondent

AFTER TWO or three centuries of fits and starts, followed by more continuous growth during the Second World War and the subsequent period of advancing marine technology, oceanography has settled down to earn its living and recent attempts to learn more from its past seem to be one of the signs of maturity. The first international congress on the History of Oceanography was held at Monaco in 1966, partly to celebrate the work of Prince Albert I of Monaco, who made extensive studies from his own research ships and built and endowed his own research centre—the Musée Océanographique—at Monaco. The second congress was held at Edinburgh from September 12–20, 1972, to celebrate the centenary of the sailing of HMS Challenger round the world on a voyage of scientific exploration. It was also the 50th anniversary of the death of Prince Albert I.

At the opening session Sir Maurice Yonge spoke on the inception and significance of the Challenger Expedition and Dr Daniel Merriman, former Master of Davenport College, Yale University, gave a graphic account of the personalities of the youngest and oldest scientists in the ship, and of life and work on board. Dr Harold Burstyn, of the Carnegie-Mellon University, Pittsburgh, showed how the scientists of the day negotiated with the Royal Society, the Admiralty and the Government and how the problems which still face marine science were dealt with 100 years ago. Eighty papers were presented on the following days, one of which by Dr D. E. Cartwright of the National Institute of Oceanography at Wormley showed how the results of a continuous series of tidal observations, made with remarkable perseverance of effort and accuracy at Brest from 1711 to 1716 by Cassini, were lost for 50 years before being found, with great difficulty, incomplete and without relevant meteorological information by Lalande, who published the data, which were afterwards used by Laplace, who pioneered rigorous methods of tide prediction.

One of the most telling coloured slides was shown at the congress by Mr P. Foxton of the National Institute of Oceanography. It showed one of the twelve, charred, surviving pages of the late Dr Stanley Kemp's revision of the *Acanthephyra*, which was recovered after the disastrous bombing of the Plymouth laboratory during the Second World War. All the presented papers have been published in volumes 72 and 73 of the Proceedings (Section B) of the Royal Society of Edinburgh. A feature of the congress was the different way the

historians and scientists approached the history of oceanography. The historians tended to have a systematic approach whereas the scientists' approach could be called subjective dabbling. But the scientists did give some of the most effective contributions and it was clear that they are finding historical studies well worth while.

The congress was made possible by collaboration between the Royal Societies of Edinburgh and London, with generous support from the City and University of Edinburgh, and donations from many people and industrial organizations. The descendants of Sir John Murray, who succeeded Sir Wyville Thomson as Director of the Challenger Expedition Commission, were among the congress members.

CHEMISTRY

Probing Decaborane (14)

from a Correspondent

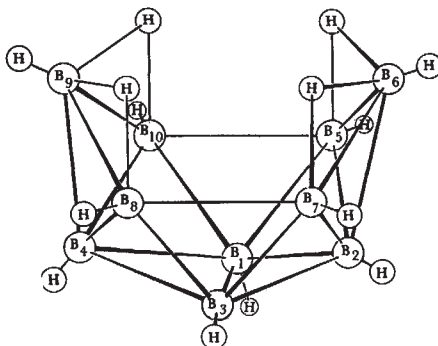
ONE of the most complex computer calculations of the electronic properties of a molecule yet attempted concerns the basket-shaped molecule $B_{10}H_{14}$ (Laws, Stevens and Lipscomb, *J. Amer. Chem. Soc.*, **94**, 4467; 1972). The molecule has little symmetry to simplify the calculation but an important advantage over calculations on more symmetrical large molecules, such as octahedral chromium hexacarbonyl and cage-shaped boron compounds (see *Molec. Phys.*, **22**, 1025; 1971; and *J. Amer. Chem. Soc.*, **92**, 4158; 1970), is that a wealth of experimental information is already available on the chemical reactivity of its various parts.

The ten boron atoms lie near corners of a regular icosahedron, omitting two corners which define a single edge, and each bears a single, terminal hydrogen atom. The remaining hydrogen atoms each bridge a pair of boron atoms, so as to "stitch up" the open face of the basket, the overall symmetry being that of V-shaped molecules such as water (point group C_{2v}). There are consequently nine distinct types of atom, namely the four sets (B_1, B_3), (B_2, B_4), (B_5, B_7, B_8, B_{10}) and (B_6, B_9) and their

respective terminal hydrogen atoms and, lastly, the set of bridging atoms ($H_{36}, H_{67}, H_{89}, H_{910}$).

In the calculation of Laws *et al.* a minimum basis set of Slater-type atomic orbitals was first chosen. These are convenient mathematical functions used to describe the electronic properties of individual component atoms of the molecule; their significance is that, if the functions "occupied" by electrons are squared and added together, the sum will be an electron density map for the atom. Linear combinations of these atomic orbitals give rise to a set of molecular orbitals (MOs), from which an electron density map of the molecule may be calculated after allocating the electrons available, usually in pairs, to the MOs of lowest calculated energy. The relevant coefficients are unknown at the start of the calculation and so a trial set has to be chosen and successively refined in accord with each calculated electron density map until successive iterations lead only to insignificant changes in both the calculated molecular orbital coefficients and the density map. This is known as the Hartree-Fock self-consistent field procedure.

The $B_{10}H_{14}$ calculation required no less than 18 h of computing time (the number of integrals calculated was 560,000), and the total energy of the molecule and that of the most readily ionized electron were predicted accurately. Conversely, and typically for such calculations, the dipole moment was overestimated by 40 per cent, but the calculated electron density agrees well qualitatively with data available from X-ray and neutron diffraction experiments. From the calculated electron density contour maps it was possible to establish the presence of a strong single bond between B_3 and B_6 , whereas the connexion between B_5 and B_6 apparently involves only hydrogen bridge bonding. The electron density in the plane $B_1B_3B_5$ was found to be almost symmetrical, which establishes the presence of a closed three-centre bond in this face (that is the face is bound by a single, symmetrically arranged pair of electrons). In the plane $B_2B_5B_7$ there is an open three-centre bond with no connexion between B_5 and B_7 . It is, however, still uncertain whether the bonding in the plane $B_1B_5B_{10}$ is closed or whether B_5 and B_{10} are disjoint. The effective static atomic charges and the electron populations of frontier orbitals (the highest occupied and lowest unoccupied MOs) are in good agreement with the experimental order of reactivity in electrophilic and nucleophilic substitution reactions—electron densities calculated for the unique boron atoms follow the sequence $2 > 1 > 5 > 6$ (Lipscomb, *Boron Hydrides*, W. A. Benjamin, New York, 1963).



Forty-five Varieties of Research (and Development)

LORD ROTHSCILD

Trinity College, Cambridge

Lord Rothschild presents his personal views about the terminology used to describe research and development.

MANY members of my family have collected things—old books, old masters, fleas, coins, old buttons and bird skins, to give a few examples. Perhaps there is a gene which determines this ubiquitous propensity, instead of the alleged chrysogene. I am no exception and recently have made a collection of different sorts of research and development, forty-five to be precise.

During the discussion, or perhaps one should say controversy, which followed the publication, in 1971, of the government's Green Paper *A Framework for Government Research and Development*¹, several people commented on the number of different sorts of research and development there seemed to be and the confusion they caused, at any rate in the minds of some people. The Select Committee on Science and Technology went so far as to recommend a special study of the problem with a view to drawing up "standard definitions for research and development"². The purpose of this article is to help to remove the confusion.

Clarification and Classification

Before the forty-five different varieties are listed and discussed, there is some undergrowth which needs clearing out. Perhaps it is best to start by saying what research is, but there will almost certainly be differences of opinion even about this apparently straightforward matter. Sir Brian Flowers (private

letter, April 4, 1972) has this to say about research: "If what you expected was always the result of research, there would be no point in doing research, only in having expectations. Thus research is done in order to find out departures from expectation. Hence the unexpected is the whole point of scientific research". I believe this description to be ingenious but mischievous, if only because there are so many research projects which are not done to discover departures from expectation. On the contrary, much research is done to confirm a hypothesis, the opposite of a departure from expectation. It is, I believe, better and more logical to define or describe research as "a human activity, often involving experiments, designed to generate new information". The word "human" is included because it may be that in the future, machines will be able to do some forms of research (which will then, of course, not only be a human activity), if they cannot already.

Other undergrowth which must be got out of the way before considering the taxonomy of research is made clear by the following questions.

Who wants a classification of research? Is it the layman, the research worker, or the layman who is reasonably well informed about science? As in the case of a classification of plants or animals, one concerned with research must be tailored to the audience; and it is difficult, if not impossible, to cater for all the audiences at the same time without insulting some and confusing others. At the present time the most important audience consists predominantly of those laymen who are reasonably well informed about science. Ideally, of course, we should all, laymen and scientists, speak the same language; but as this counsel of perfection will not be realized in measurable time, we must have a dictionary as well as a classification.

Table 1 Forty-five Varieties of Research and Development

PURE RESEARCH S_1	APPLIED RESEARCH S_2	DEVELOPMENT S_6	MISCELLANEOUS
Basic science S_1	Absolutely applied research S_2	Generic work S_6	Self-chosen research S_7
Fundamental research S_1	Commissioned research S_2		Curiosity-oriented research S_7
Pure basic research S_1	Mission-oriented research S_2		Speculative research
Basic research S_1	Objective-oriented research and development		General research (surcharge)
Absolutely pure research S_1	Orientated research S_2		
	Product-oriented research S_2		
	Tactical science S_2		
	Target research S_2		
	Applied (project) research		
	Applied (operational) research		
	Short term "trouble shooting" research		
	Exploratory research		
	Product research		
	Process research		
	Method of operation research S_3		
	Operational research S_3		
	Strategic research S_4		
	Other strategic research S_4		
	Strategic science S_4		
	Basic strategic research S_4		
	Strategic research C S_4		
	Objective basic research S_5		
	Target basic research S_5		
	Targeted basic research S_5		
	Basic applied research S_5		
	Applied basic research S_5		
	Strategic applied research S_5		
	Applied strategic research S_5		
	Oriented-strategic research S_5		
	Underlying research S_5		
	Strategic research A S_5		
	Strategic research B S_5		

$S_1, S_2 \dots$ = synonyms. See glossary for further descriptions or definitions.

What is the object of the classification? Animals and plants are classified for two reasons: first, because certain groups of plants and of animals exhibit similarities which merit a word which encompasses these similarities. Examples are "fish", "ferns" and "mammals", or their Latin equivalents. The second reason is because it is neither meaningful nor possible for a human being to cope with the animal or plant kingdom in terms of the individual species, of which there are more than a million, that go to make up these kingdoms. Classification, in other words, is a necessary distillation or simplification of otherwise indigestible information and is needed to facilitate the public (or private) discussion, by laymen and scientists, of scientific policy.

Should the classification take into account who wants the research done? The question is, obviously, different from the first one. If the answer is yes, the words or phrases in the classification may be different, or may have a different meaning from what they would have in the absence of a positive answer to the question. A case in point is the scientist who decides to research on a new sort of milking machine. Such research is self-chosen, which some people seem to believe is a better phrase than pure research. Nevertheless the work is obviously applied.

Should the classification take into account why and how the research is done? The answer to the former is, I believe, yes, and although in principle the answer to the latter is no, in practice there may be occasional exceptions.

Forty-five Varieties

The forty-five "different sorts" of research and development are listed in Table 1. It is important to start by saying, as I have done on two occasions before, that provided one defines whichever phrase is used and provided a definition is not internally contradictory, the actual phrase used is of secondary importance. Nevertheless, the definition may be internally consistent but liable to cause confusion, for example, again, self-chosen research. Furthermore, descriptions can be of such generality as to be of questionable value (except to score points), even though they may be meaningful in certain respects. An example in this category is the statement that "all research forms a continuous spectrum. There is no such thing as one particular type of research in contradistinction to another". It is unnecessary to say much about this statement, which I have used to advantage from time to time, other than that if someone does not know that object A is yellow and object B is blue, there is something wrong with his eyesight.

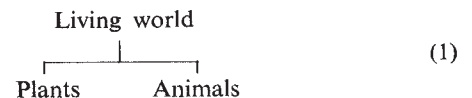
Table 1 has four columns. The first, third and fourth are, I hope, self-explanatory, at any rate if studied in conjunction with the glossary at the end of this article. Both in this table and in the glossary, pure research, in the first column, is preferred to its synonyms. As noted in the Zuckerman Report³, the synonyms fundamental research and basic research, particularly the former, have a somewhat grandiose connotation which is not often justified by the research in question. The second column is divided into four sections. The first of these contains synonyms for applied research, and the second contains subdivisions of applied research. The third section includes the "purest" forms of strategic research, and the fourth the less "pure" varieties. The whole subject of strategic research is discussed later.

Semantics

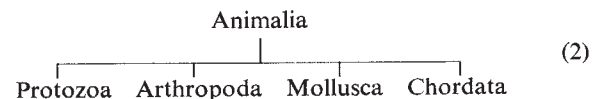
It is more difficult for the layman than the professional to understand some of the nuances in research terminology. To cite an analogy from elementary mathematics, the professional who knows that $a^2 + b^2 = (a + ib)(a - ib)$ will not mind if it is written $a^2 + b^2 = (a + jb)(a - jb)$. He may just note that the person who wrote the second equation could have been an electrical engineer. Whoever understands the equation will not be troubled by the substitution of a j for an i . As a matter of fact, if some lunatic wrote $a^2 + b^2 = (a + \pi b)(a - \pi b)$, every professional would know that in this case, π equalled $\sqrt{-1}$

and not 3.1416. Similarly, the professional will not or should not be troubled by pure, basic, fundamental, pure basic or absolutely pure research, and will understand that all five phrases mean the same thing. But curiosity-oriented and self-chosen research are not necessarily the same as pure research because a scientist's curiosity or personal choice may lead him to research on a new form of milking machine, a form of research which everyone would categorize as applied, applied (project), product-oriented, tactical, mission-oriented, objective oriented, orientated or applied (operational) research. Self-chosen research on a new milking machine would not, of course, be commissioned research because the scientist chose, rather rashly, to do it himself. Rashly, because what may appear successful to the scientist may cause him considerable frustration when, for good reasons previously unknown to him, the results of his research are not utilized.

Lord Jellicoe⁴ referred to the "ghastly semantic jungle" of research terminology. This jungle has been created by, first, inadequate appreciation of the difference between a dictionary and a classification; second, inadequate attention to definitions or descriptions (which form part of the dictionary); third, the invention or use of unnecessary synonyms; and, fourth, the invention or use of ambiguous phrases or ones which are liable to be misunderstood. Before revising Table 1 in the light of these four points, it may be useful to examine very briefly the difference between a classification and a dictionary. An incomplete classification of the living world might be depicted as follows:



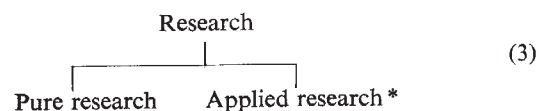
An even more incomplete classification of animals might be



Each of the subdivisions mentioned in classification (2)—in reality there are about twenty-three—can be subdivided into classes, orders, genera and species. One can define or describe Protozoa as animals (naturally) whose bodies have not got a multicellular structure. Within the Protozoa (if one wants to be more sophisticated) there are six classes, one of which, Rhizopoda, contains the genus *Amoeba* which is described or defined as Protozoa (naturally) which move by means of pseudopodia.

Those concerned with the classification of living organisms, taxonomists, quite often disagree with each other. Some, for example, believe that sponges (Porifera) are a subdivision of the animal kingdom, like Protozoa; others think they are a sub-kingdom within the kingdom Animalia, that is "above" Protozoa and the rest, but not directly related to them; while a few even consider they are a separate kingdom like plants. Differences of opinion also arise about which part of the classification a particular animal should be assigned to. It is not, however, possible for an animal to be assigned to two different places at the same time. But this may not necessarily be true in the case of the classification of research. The differences of opinion about animal classification mentioned above are not of great importance provided the characteristics of the group of living organisms are described or defined in a reasonable, unambiguous and acceptable way.

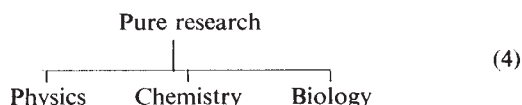
Translating this digression into the subject under consideration, the following initial classification of research seems reasonable:



* Some people prefer applied research and development to applied research. I can see no objection to this preference.

As mentioned earlier, research is a human activity, often involving experiments, designed to generate new information. Pure research is done solely to increase knowledge. It is often motivated by curiosity and does not have any application in view. Applied research, on the other hand, is done with a potential or actual application (or use) in view, as its name implies. All research done with some goal beyond that of gaining new information is defined as applied.

There are several ways in which pure research can be subdivided. One is by subject, for example:



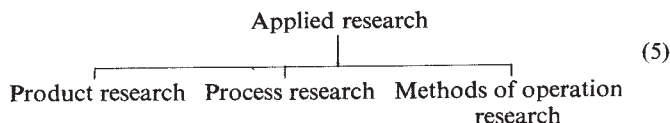
after which chemistry might be subdivided into theoretical chemistry, physical chemistry, inorganic chemistry, organic chemistry and even, perhaps, semi-organic chemistry. A number of people, particularly, I believe, among scientists, might question the value of dividing pure research into physical, chemical and biological research on the grounds that the concepts and techniques of physics and chemistry are constantly used in biology and because the same applies to physics and chemistry, as evidenced by such phrases as chemical physics. While therefore the division into physics, chemistry and biology may still have value at the student level, it has less meaning in research than it did fifty years ago and may have even less in fifty years time.

An alternative subdivision of pure research can be made into pure basic research and objective basic research, which is the Zuckerman terminology³. These phrases relate to the question why the research is done. Pure basic research is identical with pure research as defined above; but "basic" is a synonym for "pure", whereas "pure", as used by Zuckerman, has its normal meaning—unadulterated, unsullied, untainted and so on. These considerations militate against the use of the term pure basic research. Indeed, the reader will observe that in the glossary at the end of this article, most of the terms listed are followed by a recommendation that they should not be used.

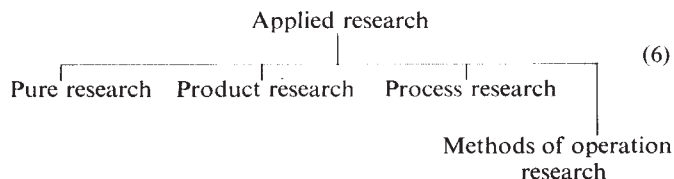
There are two objections to the phrase objective basic research which, given that "basic" is identical with "pure", could equally well be objective pure research. First, the word "objective" is slightly ambiguous in that it can either refer to an objective (the intended use of Zuckerman); or it can mean dispassionate. Apart from this ambiguity the objective of a research project might just as well be the advancement of knowledge (pure research), as the attempt to realize a practical objective (applied research). It seems therefore that objective basic research as a subdivision of pure research, or as a category in its own right, is of questionable value. Moreover, I believe that objective basic research is indistinguishable from strategic research. Both of them are pure research, done within an applied research field, however imprecisely formulated, to get information without which the ultimate objective of the applied research cannot be fulfilled. It seems therefore that no subdivisions of pure research in classification (3) are necessary or desirable, unless one wants to enumerate the so-called different scientific disciplines such as physics, chemistry and so on, which is not the object of the exercise.

Applied Research

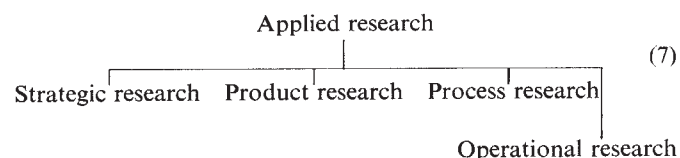
We must now turn to the other limb of classification (3), applied research, which has already been defined. This can be subdivided, as by Rothschild¹, as follows:



While it may be obvious to some that pure research, which is quite separate from the general research surcharge (see glossary), may be undertaken within all or any of these three subdivisions, it has certainly not been obvious to many scientists and laymen. Consequently, there is a case for altering classification (5) to



Two comments may be made about classification (6): first, pure research is identical, as mentioned earlier, with objective basic research and strategic research as defined by Dainton¹. Second, it is identical with pure research in classification (3). This is logically correct because whether pure research is done in its own right or as part of an applied research programme, the way the work is conducted is identical in both cases. The programme and behaviour of a scientist studying the effect of small concentrations of polymers of high molecular weight on the turbulent flow of liquids along a tube will be the same whether he wishes to gratify his own curiosity or if those sponsoring the research are ultimately interested in the economics of oil pipelines. Nevertheless, there is or may be a difference between pure research (classification (6)) and pure research (classification (3)): it concerns the time scale. Pure research within an applied programme should have a date structure, though it may be a long one. One can, for example, imagine that a reappraisal of the pure research programme might be desirable every five years, if only because the realization of the applied research project at the wrong time might make it valueless. It would not have been of much use to have produced the Wankel engine at some time during the next century when there may be little or no fuel available for it. Because of this difference between pure research (6) and (3)*, there is a case for substituting strategic research for pure research in classification (6). Operational research should replace method of operation research, so that classification (6) becomes



Although, as mentioned above, strategic research can be part of product research, process research and, even, operational research, the overwhelming desire of scientists in the United Kingdom to use the phrase is a sufficient reason for doing so. But it is scarcely necessary or desirable, at any rate in the context of this article, to have three different sorts of strategic research, A, B and C, as proposed by T. L. V. Ulbricht (ARC Planning Section). In any case his strategic research C is identical with strategic research, apart from containing the undesirable phrase "of an open-ended nature".

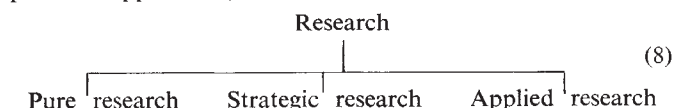
Rationalizing the Classification

It is now possible to construct a reasonably simple and intelligible classification of research, but before doing so, I must discuss the reason why certain phrases are excluded even though they are not synonyms. There seems little reason to retain Zuckerman's applied (project) research. His definition of it, in the glossary, shows that it is neither product, process nor operational research, though the examples cited as illustrations all fit into one or other of these three categories. The

* I do not, however, believe that any pure research project should be "open-ended" in time, as proposed in the description of strategic research C (see glossary).

same applies to applied (operational) research because the examples given show that it is either process research or operational research. It is therefore ambiguous. Short term "trouble shooting" research is not worth inclusion in a classification as opposed to a book on the subject. In any case "trouble shooting" may not be research at all. Exploratory research, though a popular phrase in industry, refers, as Zuckerman said, to semi-empirical experimentation during the identification of a problem or project. As it can apply to any part of classification (7), it has been omitted.

We now come to the fourteen "types" of strategic research. It is obviously possible to detect and identify nuances between such phrases as basic strategic research and strategic applied research; but it is questionable whether these distinctions are meaningful in the present context or, for that matter, at all. In all cases reference is made to pure research within an applied research programme. If, inconceivably, it is held that strategic research, basic strategic research and strategic research C have nothing to do with applied research, they are identical with pure research and there is no point in inventing new names for it. One can, of course, modify classification (3) even if there is a hope or chance that the work may have some practical application, so that it becomes



But there is no justification in logic for this course of action.

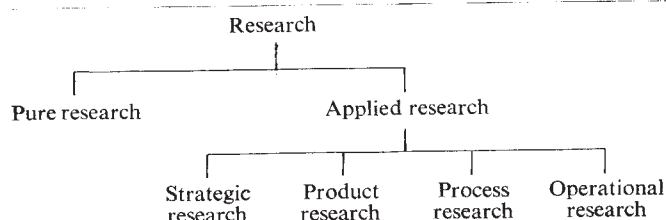
Dainton uses the word science instead of research. As science includes teaching and learning (in the school sense), whereas research does not, and it is research that is under the microscope here, the word science is inappropriate and should not be used in this context. This in no way implies that the research councils are not concerned with science, just as other organizations such as schools and colleges are. It is important to emphasize that as science is not identical with research, the same classification may and, in fact, will not be appropriate for both; and the same applies to glossaries relating to these two subjects.

Dainton's tactical science should be rejected even if changed to tactical research, apart from it being a synonym of applied research. There are two reasons. First, because in its definition or description, there is a reference to such work being undertaken to further the "immediate executive or commercial functions" of departments of state and industry. The use of the word "immediate" reveals a misunderstanding both of the functions of departments of state and industry and of the nature of applied research. Second, it is hardly tactful to say that "at the other extreme", it (presumably tactical science) "amounts to little more than a modest intelligence" (*sic*).

None of the entries under "miscellaneous" in Table 1 should be included in a classification of research, though some remarks about them will be found in the glossary.

We are now in a position to construct a reasonable, unambiguous and, hopefully, acceptable classification of research. This is done in Table 2, which, even if unacceptable, may, together with this paper, stimulate others to produce an improved version.

Table 2 A Classification of Research



This classification does not preclude pure research being undertaken within a product, process or operational research programme. Strategic research is defined in the glossary.

International Terminology

In its first report², the Select Committee recommended that the Council for Science and Technology which it proposed should be set up "should collaborate closely with international standard-making bodies such as OECD and should take account of foreign practice in drawing up standard definitions for the United Kingdom" (page iv, recommendation 8). The most obvious way of examining this question is by comparing what is said and recommended earlier in this paper with the recommendations in the "Frascati Manual" *The Measurement of Scientific and Technical Activities*, published in 1970 by OECD (DAS/SPR/70.40). The classification used in this manual is basic research, divided into pure basic research and oriented basic research; applied research (whose definition is questionable); and experimental development. All but the last of these phrases have been discussed and analysed earlier in this article or will be dealt with in the glossary. Experimental development is defined as "the use of scientific knowledge in order to produce new or substantially improved materials, devices, products, processes, systems or services" (page 10, "Frascati Manual"). On page 9 of the manual there is a footnote stating that "The adjective 'experimental' was adopted for the 1968 revision of the Frascati Manual, (a) to avoid a confusion between 'development', a phase of research and development activities, and the same term in economics, and (b) to use the same term as Eastern European countries and UNESCO." It is not clear whether experimental development, its definition and the explanation of its *raison d'être* have been accepted; but if they have, it is hard to understand why. A definition of development, due to Zuckerman³, is given in the glossary and it will be seen that whatever this word may mean in economics, in this context it is inevitably experimental. One might add to the glossary entry that development is invariably much more expensive than research and that it should not be started unless there is a 0.9 or, even, 0.95 probability that the outcome will be successful, for example that production will follow.

The definition of experimental development, quoted above, is indistinguishable from applied research as defined in the glossary. But it is not indistinguishable from applied research as defined in the "Frascati Manual"—"Applied research is also original investigation undertaken in order to gain new scientific or technical knowledge. It is, however, directed primarily towards a specific practical aim or objective". As everyone knows, the production of new materials, products and devices—experimental development—has called for a very high level of originality and creativity; but according to the manual, they do not, though applied research, which apparently is something different, does need "original investigation".

The conclusion seems inescapable that the three categories of research and development proposed in the "Frascati Manual" should not be accepted, except for the first category, basic research, which I believe could advantageously be replaced by pure research.

Glossary

ABSOLUTELY APPLIED RESEARCH⁵ *

It is not quite clear whether the Select Committee on Science and Technology intended to use this phrase, as they did absolutely pure research, or not. (Do not use.)[†]

ABSOLUTELY PURE RESEARCH⁵

(Do not use.)

APPLIED BASIC RESEARCH

Synonym for strategic research. (Do not use.)

* No reference number means that the phrase is in common usage or that the originator is not known.

† Recommendation (here and elsewhere).

APPLIED RESEARCH

Research done with a potential or actual application (or use) in view.

APPLIED (OPERATIONAL) RESEARCH³

Applied research directed to improving the use of an existing process or piece of equipment.

"An example is the improvement of the working performance of an existing type of graphite-moderated carbon dioxide-cooled nuclear reactor; or the provision of the data for improving the design and lay-out of farm buildings by a study of their purpose and day-to-day use." (Do not use.)

APPLIED (PROJECT) RESEARCH³

Applied research has as its object the attainment of a practical goal such as a new process or piece of equipment.

"An example is the provision of design data for a nuclear-powered submarine or the determination of the cause of the specific failure of a particular crop and the derivation of a remedy to prevent its recurrence." (Do not use.)

APPLIED STRATEGIC RESEARCH⁶

"Research carried out to provide essential understanding of a current applied project."

This is stated to be a synonym for oriented-strategic research, but is in any case a synonym for strategic research. (Do not use.)

BASIC APPLIED RESEARCH

Synonym for strategic research. (Do not use.)

BASIC RESEARCH

Synonym for pure research. (Do not use.)

BASIC SCIENCE¹

"Research and training which have no specific application in view but which are necessary to ensure the advance of scientific knowledge and the maintenance of a corps of able scientists, on which depends the future ability of the country to use science." (Do not use.)

BASIC STRATEGIC RESEARCH⁷

"Background investigation which may or may not help in reaching one or a number of objectives, that is work which could logically lead to applied research and development but may not." Synonym for strategic research. (Do not use.)

COMMISSIONED RESEARCH⁸

Synonym for applied research. (Do not use.)

CURIOSITY-ORIENTED RESEARCH⁹

May be pure, applied or anything else. Synonym for self-chosen research. (Do not use.)

DEVELOPMENT³

"Development bridges the gap between research and production. It may be defined as the work necessary to take, for example, a new process or piece of equipment to the production stage. It will often include the erection and operation of pilot plants or the construction of prototypes.

"Examples of development are: The work required to determine the best production techniques for the maintenance of solid fuel elements for a nuclear reactor, research having determined the necessary composition of the fuel elements and the material for the containers. The work required to determine the appropriate process for manufacturing penicillin on a large scale, research having established its antibiotic properties, and small-scale trials its clinical usefulness."

EXPLORATORY RESEARCH

Semi-empirical experimentation, usually within an applied research programme. (Do not use as a formal research designation.)

FUNDAMENTAL RESEARCH

Synonym for pure research. (Do not use.)

GENERAL RESEARCH (SURCHARGE) (Rothschild¹)

Research which may be pure or applied and which is not directly concerned with an applied research programme, though done by the same research group, organization or laboratory.

Not part of the research classification under consideration.

GENERIC WORK¹⁰

Work aimed at "proving" a reactor system to the stage of demonstrating that it can provide a commercially viable method of power generation. Synonym for development. (Do not use.)

METHOD OF OPERATION RESEARCH¹

Synonym for operational research. (Do not use.)

MISSION-ORIENTED RESEARCH

Synonym for applied research. (Do not use.)

OBJECTIVE BASIC RESEARCH³

"Between 'pure' and 'applied' research there lies an intermediate category of scientific work to which we have given the name 'objective basic'. This denotes basic research in fields of recognized potential technological importance. It is well known that the pursuit of defined technological objectives, for example the development of a supersonic aircraft, sometimes exposes an area in which existing scientific knowledge is seriously insufficient. It then becomes necessary to try to organize an increase in this knowledge before a further technological advance can be made. Research of this type may be as intellectually exacting as what we have called 'pure basic' research. The difference between 'pure basic' and 'objective basic' research derives mainly from the fact that the latter is stimulated primarily by technological needs. It therefore calls for a planned approach even when the satisfaction of these needs is remote. This characteristic of 'relevance' to a definable technological objective is a practical criterion which differentiates 'objective' basic research from 'pure' basic research.

"Examples of objective basic research are: The study of the fundamentals of plasma physics, which may provide data likely to be of value to work on thermonuclear fusion directed to the harnessing of new sources of energy. A study of the growth of virus in living cells, which may provide information of value in combating virus infections of man."

Synonym for strategic research. (Do not use.)

OBJECTIVE ORIENTED RESEARCH AND DEVELOPMENT¹¹

Synonym for applied research and development. (Do not use.)

OPERATIONAL RESEARCH

The application of objective and quantitative criteria to decision-making previously tackled by experience, intuition or prejudice. Called operations research in the USA.

A subdivision of applied research.

ORIENTATED RESEARCH¹²

Synonym for applied research. (Do not use.)

ORIENTED-STRATEGIC RESEARCH⁷

"Background research thought likely to be necessary in order to achieve a specified objective, that is it could be an element in a widely-drawn research and development contract, though costs may not be predictable." Synonym for strategic research. (Do not use.)

OTHER STRATEGIC RESEARCH⁶

Stated to be a synonym for basic strategic research and is a synonym for strategic research. (Do not use.)

PROCESS RESEARCH (Rothschild¹)

A subdivision of applied research whose objective is a new or improved process.

PRODUCT RESEARCH (Rothschild¹)

A subdivision of applied research whose objective is a new or improved product.

PRODUCT-ORIENTED RESEARCH⁹

Hinton used this phrase in contradistinction to what he called curiosity-oriented research. Instead of product-oriented research, he might therefore have equally well said process-oriented research. Research aimed at inventing a new process or increasing the yield of an existing one are examples of process-oriented research. It is quite different from research done to improve an existing product or to produce a new one, both of which are examples of product-oriented research. In Hinton's sense, therefore, product-oriented research is a synonym for applied research. (Do not use.)

PURE BASIC RESEARCH³

"Pure basic research is research carried out solely in order to increase scientific knowledge: that is, knowledge of the nature of the material world. Such research is commonly called either 'fundamental' or 'pure' or 'basic'. These words, particularly 'fundamental', are often connected with the idea of work of high intellectual quality. A fair amount of 'pure' scientific research may, however, be of a routine or of a preliminary nature. For example: (i) 'filling in', where a main break-through has already been made; (ii) exploratory work in fields where a good deal of semi-empirical experimentation is needed before the real problems can be identified; (iii) descriptive observational work, notably in biology and geology. A line of 'pure basic' research is selected by the individual worker to satisfy his own tastes and intellectual curiosity. Examples of pure basic research are: A study of the properties of high energy cosmic-ray particles. The correlation of the chemical and structural changes that take place in muscle during its contraction and relaxation."

Synonym for pure research. (Do not use.)

PURE RESEARCH

Research done solely to increase knowledge, without any practical application in view.

SELF-CHOSEN RESEARCH⁸

May be pure, applied or anything else.

Synonym for curiosity-oriented research. (Do not use.)

SHORT TERM "TROUBLE SHOOTING" RESEARCH

A subdivision of applied research. (Do not use as a formal research designation.)

SPECULATIVE RESEARCH¹³

Partially synonymous with General Research (Surcharge). (Do not use.)

STRATEGIC APPLIED RESEARCH¹⁴

Synonym for strategic research. (Do not use.)

STRATEGIC RESEARCH

Research undertaken to generate specific applied programmes.

STRATEGIC RESEARCH A (T. L. V. Ulbricht, ARC Planning Section)

"Research which is required to provide understanding of a current applied project; strategic A workers either form part of the applied project team or work very closely with it."

A subdivision of strategic research. (Do not use.)

STRATEGIC RESEARCH B (T. L. V. Ulbricht, ARC Planning Section)

"Research carried out with the main aim of understanding some particular aspect of agriculture in order to generate

specific applied projects." A subdivision of strategic research. (Do not use.)

STRATEGIC RESEARCH C (T. L. V. Ulbricht, ARC Planning Section)

"Research of an open-ended nature with no specific application in view but which furthers the scientific understanding of agriculture." A subdivision of strategic research. (Do not use.)

STRATEGIC SCIENCE (Dainton¹)

"The broad spread of more general scientific effort which is needed as a foundation for this tactical science. It is no less relevant in terms of practical objectives of the sort we have mentioned, but more wide ranging. For this 'strategic' work to be successful it is necessary to maintain the vigour of the underlying scientific disciplines and to deploy these disciplines with due regard to national goals." (Do not use, but see Strategic Research.)

TACTICAL SCIENCE (Dainton¹)

"The science and its application and development needed by departments of state and by industry to further their immediate executive or commercial functions. The extent and nature of this activity may vary widely according to the functions served and to the degree that they involve science. At one extreme it may contain a significant element of sophisticated research over a long period: whilst at the other extreme it amounts to little more than a modest intelligence and advisory activity."

Synonym for applied research (or science). (Do not use.)

TARGET BASIC RESEARCH

Synonym for strategic research. (Do not use.)

TARGETED BASIC RESEARCH

Synonym for strategic research. (Do not use.)

TARGET RESEARCH

Synonym for applied research. (Do not use.)

UNDERLYING RESEARCH¹⁵

"This research is intended to provide a firm scientific base for nuclear technology—for instance in the fields of new materials development, radiation damage, nuclear physics and computational techniques. The constituent parts of it cannot all of them be precisely related to specific operational objectives . . ." Synonym for strategic research. (Do not use.)

I am greatly indebted to Professor Sir Brian Flowers, Chairman of the Science Research Council, and Mr J. E. J. Altham, Modal Logic, Cambridge University, for reading and commenting on this article. I have incorporated some of their suggestions; but the article remains my sole responsibility, in a personal capacity.

¹ *A Framework for Government Research and Development* (Cmd. 4814, HMSO, 1971).

² *First Report from the Select Committee on Science and Technology—Research and Development*, xv, para 58 (HMSO, 237, 1972) (called *Select Committee I* or analogous designations in subsequent references).

³ Zuckerman, Sir Solly, *The Management and Control of Research and Development* (HMSO, 1961).

⁴ *Select Committee I*, xv, para. 54 (1972).

⁵ *Select Committee I*, xv, para. 56 (1972).

⁶ *Select Committee I*, xxxv (1972).

⁷ *Select Committee I*, xxxvi (1972).

⁸ Cottrell, Sir Alan, *Select Committee Minutes*, 389, para. 1487 (HMSO 114-xi, 1972).

⁹ Hinton, Lord, *Hansard*, 328, No. 44, column 885 (HMSO, 1972).

¹⁰ *Select Committee Minutes*, 25, para 7 (HMSO 239-ii, 1972).

¹¹ *Select Committee Minutes*, 24, para. 4 (HMSO 239-ii, 1972).

¹² *Select Committee I*, xv, para. 53 (1972).

¹³ *Select Committee I*, xxxi, para. 163 (1972).

¹⁴ *Memorandum by the Council of the Royal Society on the Consultative Document* (Cmd. 4816), "A Framework for Government Research and Development" (Appendix 2, Report of the Industrial Activities Committee of the Royal Society, February 1972).

¹⁵ *Select Committee Minutes*, 25, para. 11 (HMSO, 1972).

Vertebrate Faunas and Chronology of Hominid-bearing Sediments East of Lake Rudolf, Kenya

VINCENT J. MAGLIO

Department of Geological and Geophysical Sciences, Princeton University, Princeton, New Jersey 08540

The vertebrate faunas which have been collected from east of Lake Rudolf include hominid remains and the earliest dated stone artefacts known. It is now possible to recognize faunal units and to establish a tentative chronology for observed faunal events. It is suggested here that the faunal sequence at East Rudolf may extend from 4.5 m.y. to about 1.3 m.y. with a significant break between about 4.0 and 2.6 m.y.

THE Ethiopian biogeographic region contains the most diverse assemblage of large mammals to survive into the Recent epoch¹. Valuable evidence relating to the early antecedents of this fauna is now emerging from palaeontological work in the Lake Rudolf basin. This article summarizes some of the results obtained during the past several years by expeditions under the coordination of Richard E. Leakey and the National Museums of Kenya.

More than forty-five hominid specimens have been recovered from the East Rudolf exposures, and these remains seem to represent the two taxa *Australopithecus* sp. and *Homo* sp.^{2,3}. Furthermore, a tuff bed dated by the potassium argon method at 2.6 ± 0.26 m.y. (ref. 4) has yielded the oldest known stone artefacts and hominid occupation sites^{5,6}.

The East Rudolf exposures outcrop along a broad belt some 20 km wide from the police border post at Ileret southward 70 km to Alia Bay. Fig. 1 shows the geographic distribution of collecting localities for fauna and artefacts. Stratigraphic relationships have been investigated by A. K. Behrensmeyer⁷ and a team from Iowa State University (ref. 8 and C. F. Vondra *et al.*, in preparation) (see Fig. 2). Three subregions have been recognized—Kubi Algi, the Koobi Fora Ridge, and Ileret—but mapped lithostratigraphic correlations between these subregions have not yet been firmly established. Within each subregion areas of sediment outcrop have been designated by a numerical reference system as follows: Ileret, 1–99; Koobi Fora Ridge, 100–199; Kubi Algi, 200–299.

The Vertebrate Faunas

More than 1,000 fossil specimens have been collected and assigned to local stratigraphic units (see Table 1). Several species are known in the collection by a single specimen of uncertain provenance; these are listed separately in the first

column. For most species no attempt has been made to distinguish between recognizable evolutionary stages.

Several taxa show a significant degree of change through the stratigraphic sequence. These groups are represented by successive stages within the evolution of a presumed single lineage⁹ and can be used for faunal correlation. The three most important species for this purpose are the suids *Mesochoreus limnetes* and *Metridiochoreus andrewsi*, and the elephant *Elephas recki*. It may become necessary to divide such long lineages under discrete species names but at present

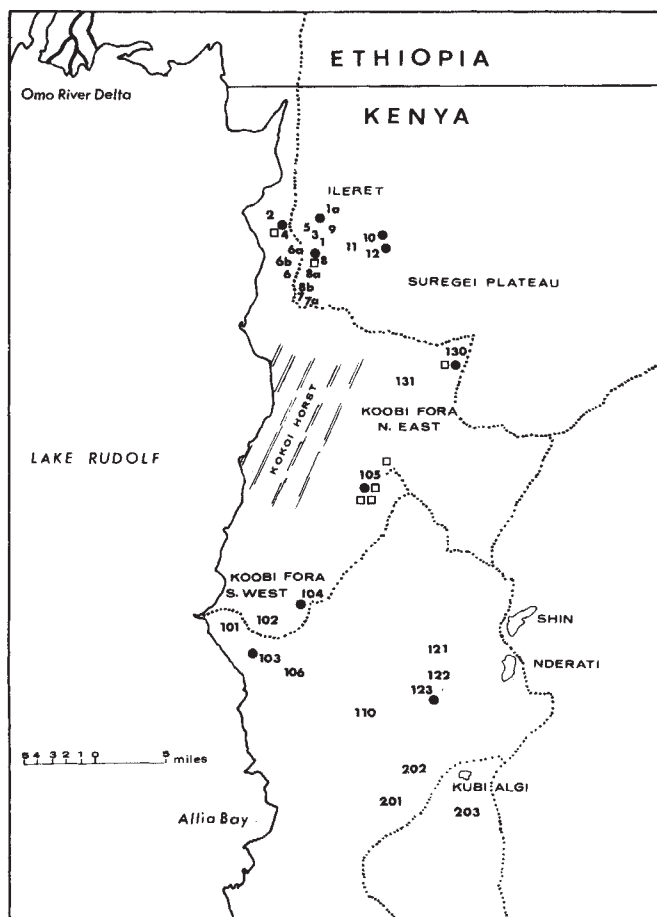


Fig. 1 Eastern Lake Rudolf, Kenya. The approximate distributions of principal localities of hominid and archaeological sites are shown in relation to the major collecting areas. ●, Hominid site; □, archaeological site.

Table 1 Tentative Faunal List from East Lake Rudolf, Kenya (Faunal Zones and Areas of Occurrence are Given for each Taxon)

	Faunal * zone	?	1	1A	3	6	6A	7	7A	8	8A	8B	10	101	102	103	104	105a	105b	120	121	122	123	130	201	202
Bovidae																										
<i>Damaliscus</i> sp. nov.	1, 2												x				x									
<i>Damaliscus</i> cf. <i>niro</i>	1, 2, 3		x				x					x				x										
<i>Connochaetes</i> cf. <i>africanus</i>	—		x													x										
<i>Megalotragus</i> cf. <i>kattwinkeli</i>	1, 2, 3		x		x								x					x	x							
<i>Aepyceros</i> sp.	1, 2		x				x						x				x									
<i>Antidorcas wellsi</i>	2																x									
<i>Gazella</i> sp. indet.	2																x									
<i>Pelorovis</i> cf. <i>olduwayensis</i>	1		x														x									
<i>Pelorovis</i> sp. nov.	1, 2						x	x			x	x			x	x	x									
cf. <i>Synceros</i> sp.	4																									
<i>Hippotragus gigas</i>	—		x																							x
<i>Oryx</i> sp.	—		x																							
<i>Kobus sigmoidalis</i>	1, 2, 3			x	x						x					x	x							x		
<i>Kobus</i> cf. <i>kob</i>	1, 2		x	x	x		x			x				x	x									x		
<i>Menelikia</i> sp.	1, 2						x			x								x		x				x		
<i>Redunca ancystocera</i>	2											x					x									
<i>Tragelaphus grandis</i>	2, 3		x										x				x			x				x		
<i>Tragelaphus nakuue</i>	3																	x						x		
Giraffidae																										
<i>Sivatherium</i> sp. nov.	1, 2			x						x					x		x									
<i>Giraffa</i> cf. <i>jumae</i>	1, 2		x													x										
<i>Giraffa</i> sp. (=cf. <i>stillei</i>)	1, 3		x			x				x																
<i>Giraffa</i> cf. <i>gracilis</i>	1, 2, 3		x				x			x						x	x				x					
Suidae																										
<i>Mesochœrus limnetes</i>	1, 2, 3		x	x	x	x	x	x		x	x	x	x		x	x	x	x			x					
<i>Metridiochoerus andrewsi</i>	1, 2		x	x	x		x	x	x	x	x	x	x		x	x	x		x							
" <i>Pronotochoerus jacksoni</i> "	1, 2, 3					x								x							x					
<i>Notochoerus capensis</i>	4																									
<i>Notochoerus euilus</i>	3																	x						x		
<i>Nyanzachoerus</i> sp.	4																							x		
<i>Potamochoerus</i> sp.	2											x														
<i>Phacochoerus</i> cf. <i>aethiopicus</i>	1, 2									x			x				x									
Hippopotamidae																										
<i>Hippopotamus</i> sp. nov.	1, 2, 3								x			x	x		x	x	x	x	x					x		
<i>Hippopotamus</i> cf. <i>amphibius</i>	1, 2		x					x			x													x		
<i>Hippopotamus</i> aff. <i>immagunculus</i>	1, 2, 3, 4		x			x				x			x			x	x	x						x		x
Hyaenidae																										
<i>Crocuta</i> cf. <i>crocuta</i>	1, 2		x			x			x				x			x	x				x					
<i>Hyaena</i> cf. <i>hyaena</i>	1, 2					x							x													
Canidae																										
<i>Canis</i> cf. <i>mesomeles</i>	2, 3		x												x		x	x								
Felidae																										
<i>Panthera</i> sp.	1, 2			x	x	x			x				x				x									
cf. <i>Therailurus</i> sp.	1		x																							
cf. <i>Homotherium</i> sp.	2																	x								
<i>Megantereon eurydon</i>	1, 2			x		x						x	x				x									
Mustelidae																										
<i>Lutra</i> sp.	2		x															x								

for purposes of evolutionary studies and for faunal correlation it seems best to recognize single lineages¹⁰.

Mesochœrus limnetes

The suid *Mesochœrus limnetes* is represented by six skulls and many lower jaws and isolated teeth from all stratigraphic levels. Cranial morphology is consistent in the oldest to the youngest beds from which this form is known (areas 1A, 8A, 10, 103 and 130). Dentitions associated with these skulls exhibit a decrease in relative length of the premolar series in younger stages and a concomitant increase in length and height of the third molar crown. Samples of isolated teeth from all areas confirm these trends. Three distinct size morphs from the three lithological members of the Koobi Fora Formation can be recognized. This species has so far provided the best means for relative correlation within the East Rudolf region.

The "typical" stage of the species includes within its range of variability the holotype specimen described from the Kaiso Formation in Uganda¹¹. The third molars, with an overall length of between 46 and 55 mm, are very low crowned with

a simple talon (-id) consisting of only one pair of columns. This stage is known at East Rudolf only in the lower member of the Koobi Fora Formation where it outcrops in areas 105, 122 and 130. (Area 105 is the only one in which two faunal zones can be defined and these are separated by a local disconformity. To avoid confusion these two units are referred to here as 105a and 105b.)

A more complex stage of the same species, designated as *Mesochœrus limnetes* "progressive", is known from the upper member of the Koobi Fora Formation along the Koobi Fora Ridge in areas 102, 103 and 104, and in rocks of the lower unnamed member at Ileret where they outcrop in areas 6A, 8B and 10. This stage is higher crowned than in the "typical" stage, the talon (-id) is more complex with two pairs of columns, and the overall length of M3 measures 54–67 mm.

A further stage, here termed "very progressive", has molar teeth that have even higher crowns. Cement is beginning to fill in the spaces between columns, but this feature is likely to be variable between populations. The complex talon (-id) bears three or more pairs of columns which contribute to the great overall length for M3 of 71–78 mm. This stage is so far known only from areas 1, 1A, 3, 6, 7, 8 and 8A of the Ileret Member.

Table 1—continued

	Faunal * zone	?	1	1A	3	6	6A	7	7A	8	8A	8B	10	101	102	103	104	105a	105b	120	121	122	123	130	201	202
Viverridae																										
gen et sp. indet.	1									x																
Deinotheriidae																										
<i>Deinotherium bozasi</i>	2												x				x									
Elephantidae																										
<i>Elephas ekorensis</i>	4																								x	
<i>Elephas recki</i>	1, 2, 3		x	x	x	x	x			x	x	x	x	x	x	x	x	x	x							
<i>Loxodonta adaurora</i>	3, 4																								x	
<i>Loxodonta africana</i>	1									x																
Gomphotheriidae																										
<i>Anancus</i> sp.	4																									x
Equidae																										
<i>Equus</i> sp.	1, 2, 3		x		x	x	x		x	x		x	x		x	x	x	x	x						x	
<i>Hipparion</i> cf. <i>albertense</i>	1, 2, 3		x						x								x	x								
Rhinocerotidae																										
<i>Ceratotherium simum</i>	1, 2, 3						x			x						x	x							x		
<i>Diceros bicornis</i>	1, 2			x												x			x							
Cercopithecidae																										
<i>Cercocebus</i> cf. <i>ado</i>	1, 2, 3		x	x		x	x			x							x							x		
<i>Cercopithecus</i> sp. indet.	2, 3		x														x	x						x		
<i>Colobus</i> sp.	1, 2			x						x																
Colobinae gen et sp. indet.	3																								x	
cf. <i>Papio</i> sp.	3																								x	
<i>Simopithecus</i> sp.	1, 2, 3		x	x	x	x		x	x	x		x	x	x	x	x	x		x	x	x	x	x	x	x	
Hominidae																										
<i>Australopithecus</i> cf. <i>boisei</i>	1, 2, 3		x		x	x	x			x			x			x	x	x					x			
<i>Homo</i> sp.	1, 2					x				x						x	x									
Hystriidae																										
<i>Hystrix</i> sp.	—		x																							
Thryonomyidae																										
<i>Thryonomys</i> sp.	1, 3			x	x	x				x														x		
Orycteropodidae																										
<i>Orycteropus</i> sp.	1, 2						x										x									
Reptilia																										
<i>Crocodylus niloticus</i>	1, 2, 3, 4																									
<i>Crocodylus</i> sp.																										
<i>Euthecodon brumpti</i>																										
<i>Geochelone</i> sp.																										
<i>Trionyx</i> sp.																										
Osteichthys																										
<i>Clarius</i> sp.																										
<i>Lates</i> sp.																										
<i>Polypterus</i> sp.																										
<i>Protopterus</i> sp.																										

* 1, *Loxodonta africana* zone; 2, *Metridiochoerus andrewsi* zone; 3, *Mesochorus limnetes* zone; 4, *Notochoerus capensis* zone.

Metridiochoerus andrewsi

Metridiochoerus andrewsi is the most abundantly represented suid at East Rudolf. It is known from four nearly complete crania, from numerous jaws and from isolated teeth. The skulls derive from the upper member of the Koobi Fora Formation at areas 103 and 104 and do not, therefore, include the earliest and latest members of the taxon at East Rudolf.

The dental series shows two distinct stages of evolution, which are characteristic of the upper member and Ileret Member respectively. Only one specimen is known from the lower member, but further excavations may yield a third, more primitive stage here.

The "typical" stage of *Metridiochoerus andrewsi* occurs in the upper member along the Koobi Fora Ridge at areas 102, 103, 104 and 105b, and at Ileret in areas 6A, 8B and 10. Its range of variation for all molar dimensions includes the holotype specimen from a locality near Homa Mt in Kenya. These teeth are low-crowned (40–65 mm in maximum height) and short in the antero-posterior direction. The lower canines are implanted in the jaw with the root passing obliquely backward into the symphysis. The upper canines are trefoil-shaped in

cross-section and bear five longitudinal bands of enamel. The upper stratigraphic levels in area 103 have yielded teeth with somewhat higher crowns and upper canines that are rounded in cross-section and with only one or two bands of enamel.

In the overlying Ileret Member a more evolved stage, *Metridiochoerus andrewsi* "progressive", occurs in areas 1, 1A, 3, 7, 7A, 8 and 8A. The molar teeth have high crowns (70–95 mm) and are longer than in the "typical" stage. The lower canines are implanted more vertically in the jaw; the roots do not pass backward into the symphysis. The upper canines have lost all traces of enamel and are rounded in cross-section except near the base where they retain the primitive trefoil shape. In gross form these tusks have developed a twisted curve.

The range of variation seen in the East Rudolf collection of this species includes the diagnostic features of several described genera (for example, *Afrochoerus*, *Tapinochoerus*) from other East African deposits. As more specimens are recovered it seems unlikely that this excessive generic splitting will prove justified, and I consider that the Lake Rudolf collections represent successive stages along a more or less continuous evolutionary line.

Table 2 Diagnostic Species of Four Faunal Zones in the East Lake Rudolf Stratigraphic Succession

Faunal zone	Areas of occurrence	Geological unit	Diagnosis
<i>Loxodonta africana</i> zone	1, 1A, 3, 6, 7, 7A, 8, 8A	Ileret Member, Koobi Fora Formation	<i>Elephas recki</i> stage 3-4 <i>Loxodonta africana</i> <i>Mesozochoerus limnetes</i> (very progressive) <i>Metridiochoerus andrewsi</i> (progressive) <i>Hippopotamus</i> cf. <i>amphibius</i> <i>Ceratotherium simum</i> (very progressive)
<i>Metridiochoerus andrewsi</i> zone	6A, 8B, 10, 102, 103, 104, 105b	Upper member, Koobi Fora Formation	<i>Elephas recki</i> stage 3 <i>Mesozochoerus limnetes</i> (progressive) <i>Metridiochoerus andrewsi</i> (typical) <i>Hippopotamus</i> sp. nov. (typical) <i>Ceratotherium simum</i> (progressive) <i>Tragelaphus</i> cf. <i>grandis</i>
<i>Mesozochoerus limnetes</i> zone	105a, 130, 123	Lower member, Koobi Fora Formation	<i>Elephas recki</i> stage 2 <i>Notochoerus euilus</i> (progressive) <i>Mesozochoerus limnetes</i> (typical) <i>Hippopotamus</i> sp. nov. (early) <i>Ceratotherium simum</i> (early) <i>Tragelaphus nakuae</i>
<i>Notochoerus capensis</i> zone	201, 202, 203	Kubi Algi beds	<i>Elephas ekorensis</i> <i>Notochoerus capensis</i> <i>Nyanzachoerus</i> sp. <i>Hippopotamus</i> sp. nov. (very early)

Elephas recki

As in most other Pleistocene deposits in East Africa *Elephas recki* is the most common elephant at Lake Rudolf. Some complete skulls, jaws, and many isolated teeth are known from all stratigraphic levels. Too few specimens have been collected to allow a meaningful evaluation here of the specific evolutionary trends known to characterize the species as a whole¹², although distinct changes can be seen to accompany the transition from the lowest to the highest beds in the Koobi Fora succession. Increase in molar plate number and in crown height in apparent compensation for reduced enamel thickness and consequent enhanced wear are most important trends in this species and can be seen also in the East Rudolf collection.

The most primitive stage¹³ of the species at Rudolf (*E. recki* stage 2) occurs in the lower member of the Koobi Fora Formation in areas 105a and 130. The molar crown is relatively low with a hypsodonty index (height/width $\times 100$) of 125-140. The enamel is rather thick (2.8-3.4 mm) and generally smooth on the worn occlusal surface with only slight folding in late stages of wear. There is a prominent median loop on the enamel figures. This stage is typical of the species as described from the Vogel River series from which the holotype derives¹⁴.

A more progressive stage (stage 3) is known from the upper member in areas 102, 103, 104 and 105b along the Koobi Fora Ridge and in area 10 at Ileret. This stage is characterized by molar teeth with higher crowns (HI = 145-165), and by thinner enamel which measures only 2.4-2.8 mm. The worn enamel figures are coarsely folded with irregularly spaced small loops, but usually lack the prominent median loops which are so typical of earlier stages.

In areas 1, 1A, 3, 6 and 8 of the Ileret Member a stage of *Elephas recki* which is intermediate between stages 3 and 4^{13,1} has been recovered. The hypsodonty index is 155-180 and the enamel is both very thin (1.5-2.3 mm) and intensely folded.

In addition to these three species several other taxa show distinct evolutionary trends within the East Rudolf succession. Few specimens are available so that stages have not been established. The two more important taxa in this regard are the white rhinoceros, *Ceratotherium simum*, and a new hippo, *Hippopotamus* sp. nov. (personal communication from S. Coryndon). Both species may be very tentatively subdivided into earlier and later stages as has been done for *Mesozochoerus*.

The Faunal Zones

The faunal samples from the East Rudolf deposits have been divided into four assemblages, each based on morphologically

distinct groups of vertebrates, and each being derived from a definable segment of the stratigraphic sequence. These faunal assemblages can thus be used to define biostratigraphic zones. The earliest assemblage, recognized in the *Notochoerus capensis* zone, occurs only in the deposits of areas 201, 202 and 203 in the Kubi Algi region. This fauna includes the gomphothere cf. *Anacus*, two early species of elephant, *Loxodonta adaurora* and *Elephas ekorensis*, a primitive tetraprotodont hippopotamus, and the early suids *Notochoerus capensis* and *Nyanzachoerus* sp. These elements are not known from the Koobi Fora Formation farther north and together they form a very distinct assemblage. (It is not yet certain how the Kubi Algi beds relate to the Koobi Fora Formation, but they may represent a fluvial facies of the lower lacustrine unit of the Koobi Fora Formation⁸.)

The Koobi Fora Formation may be divided into three additional faunal zones based on distinct evolutionary stages in suid and proboscidean lineages. These zones happen to correspond with three stratigraphic members of the formation which are defined lithologically (C. F. Vondra *et al.*, in preparation). The zones cannot be diagnosed with certainty on unique species content because the restriction of some species to one or two zones may prove to be the result of sampling error. Nevertheless, evolutionary stages within a number of taxa have proved useful as a basis for differentiation.

The earliest of these faunal assemblages, which defines the *Mesozochoerus limnetes* zone, includes the "typical" stage of that species as its most diagnostic component. A progressive form of the pig *Notochoerus euilus* (? = *N. scotti*) is common here as is *Elephas recki* stage 2. *Loxodonta adaurora* persists here only as a very rare element. The peculiar "East Rudolf hippo" is abundantly represented as the small, early stage. The bovid *Tragelaphus nakuae* is known so far only from this zone. What seems to be an early stage of the white rhinoceros is represented by only a few teeth, but this grade also seems to be restricted to this zone.

In the overlying *Metridiochoerus andrewsi* zone the "typical" form of *Mesozochoerus limnetes* has been succeeded by the "progressive" form. *Notochoerus euilus* is absent. The "typical" stage of *Metridiochoerus andrewsi* is a common element, as is stage 3 of *Elephas recki*. A larger, more specialized stage of the "East Rudolf hippo" occurs here. The white rhinoceros, *Ceratotherium simum*, is known from this level and seems from its dentition to represent a somewhat more evolved grade than in earlier faunal zones, but this needs confirmation. *Tragelaphus nakuae* is absent, but *T. cf. grandis* is well represented.

The highest zone in the stratigraphic succession is the *Loxodonta africana* zone, which is characterized by "very progressive" stages of both *Mesochorus limnetes* and *Metridiochorus andrewsi* and by the appearance of the extant African elephant, *Loxodonta africana*. The living hippo, *Hippopotamus amphibius*, and the modern stage of the white rhinoceros are also present. The dominant elephant is a stage of *Elephas recki* which is distinctly more evolved than stage 3. The diagnostic vertebrates from the four faunal zones recognizable at East Rudolf are summarized in Table 2.

Correlation of the Faunal Zones

Lacking an absolute chronology of dated horizons above the KBS tuff (dated 2.6 ± 0.26 m.y.) correlation of these faunal assemblages with those from radiometrically dated deposits at other African localities is at present the only means of establishing temporal limits for biological events at East Rudolf. The most useful faunal elements for correlation purposes are those that are abundant in the record and that were evolving relatively rapidly. The species *Mesochorus limnetes*, *Metridiochorus andrewsi* and *Elephas recki* are useful in this regard.

The trends in molar evolution of *Mesochorus limnetes* have also been observed for material collected in the Shungura Formation of the Lower Omo Valley⁹. The progression seen in various molar dimensions correlated with time points to an evolutionary sequence along a single lineage. Although the same species is also known to occur at the Olduvai Gorge in Tanzania and at other localities outside of the Lake Rudolf

basin, it is probably more meaningful to restrict comparisons to material from the Rudolf area alone.

In Fig. 3 observed ranges and arithmetic means for molar length of samples of *Mesochorus limnetes* (1-4) from the dated Shungura succession are plotted against time. The placement of samples on the time scale is, of course, only approximate and represents the "average age" of beds located between any two dated tuff horizons. As can be seen, the rate of molar length increase falls off between upper members in the Shungura Formation. Although this trend requires confirmation from higher levels, it is used here in constructing the interpolated mean curve.

The observed ranges and means of samples collected from the Koobi Fora Formation are indicated along the lower portion of Fig. 3 (A-C). These values are projected onto the Shungura sample curves. The mean value of samples from the *Mesochorus limnetes* faunal zone intersect the interpolated mean of Shungura samples at about 2.0 m.y., corresponding with material from Member F of that formation. Points of intersection of the East Rudolf means with the 98% confidence limits of the Shungura samples are at 2.7 m.y. and at 1.8 m.y. With caution these may be taken as very crude maximum and minimum indicated age limits for the fauna of the *Mesochorus limnetes* zone using this species only. The indicated age range includes the K/Ar date of 2.6 m.y. for the KBS tuff located within the sedimentary unit containing this fauna. It must be pointed out that such correlation depends upon the accuracy and stability of the Shungura Formation absolute chronology.

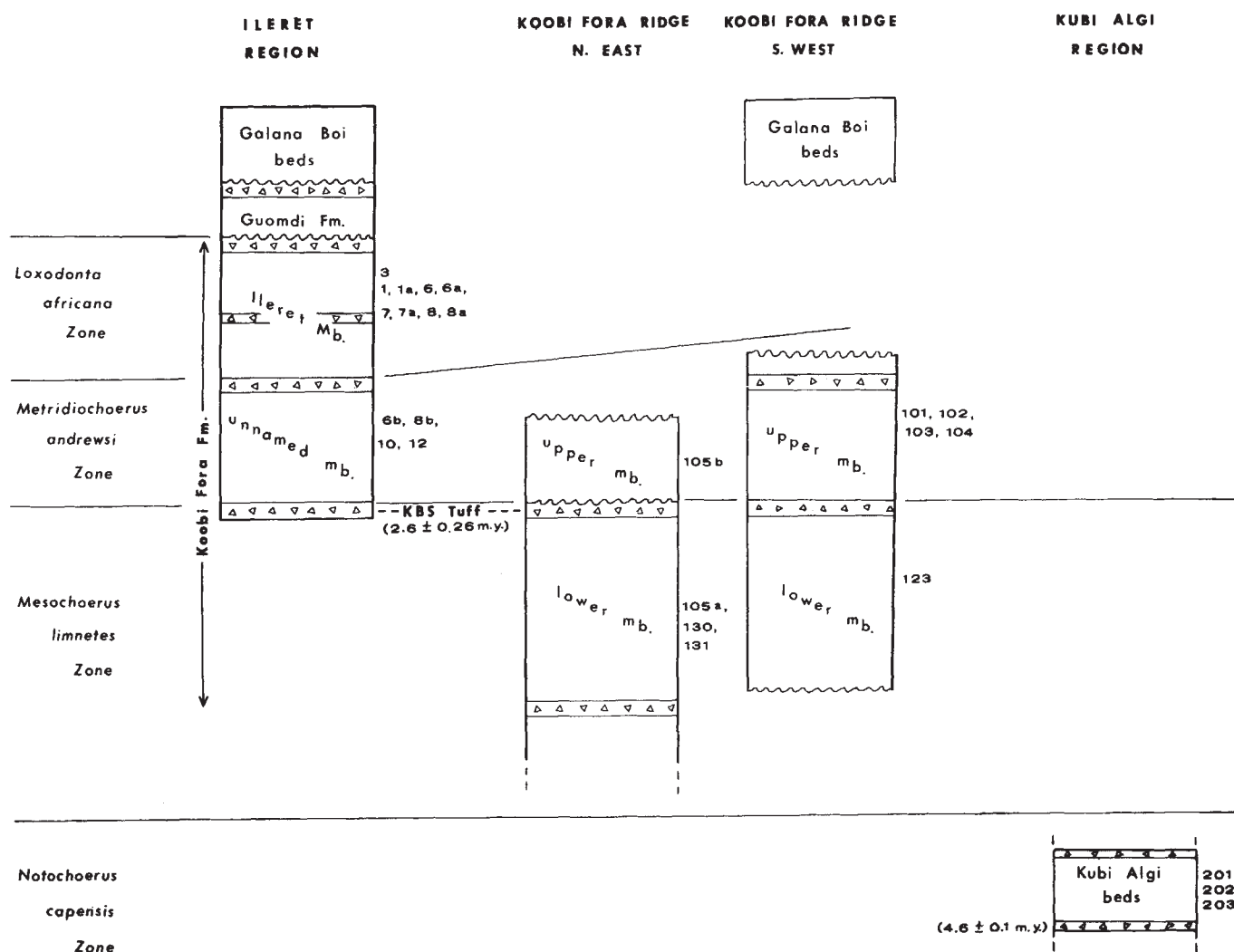


Fig. 2 Approximate correlation of lithostratigraphic units at East Rudolf and distribution of faunal zones. Major fossil collecting areas are indicated to the right of each section.

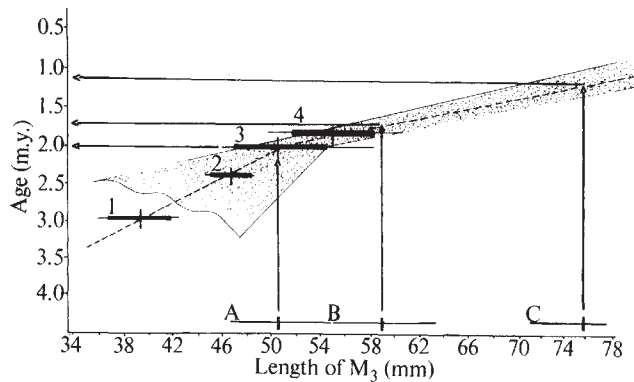


Fig. 3 Overall lengths of *Mesoschoerus limnetes* M₃ samples (1-4) from various levels in the Shungura Formation plotted against time. For each: horizontal line, observed range; vertical line, sample mean; solid rectangle, $\pm$ one standard deviation from the mean. A continuous interpolated mean (broken line) and an approximate 98% confidence limit bandwidth (shaded area) have been added. Sample ranges and means from the three faunal units at East Rudolf are plotted along the lower part of the graph (A-C). Projection of these sample means on the Shungura interpolated mean curve gives an approximate age correlation for this species.

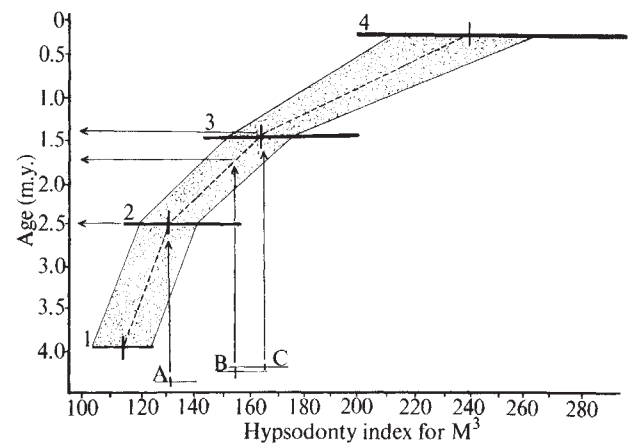


Fig. 4 Hypsodonty index for M₃ of elephant teeth in the *Elephas recki* lineage from various East African localities. For each: horizontal line, observed range; vertical line, sample mean. The interpolated mean (broken line) and 98% confidence limits (shaded area) have been added. Samples from East Rudolf faunal units (A-C) are treated as in Fig. 3.

Similar indicated mean and maximum age limits for the *Metridiochoerus andrewsi* and *Loxodonta africana* zones are 1.7 m.y. (1.8-1.6 m.y.) and 1.2 m.y. (1.4-0.9 m.y.) respectively.

In Fig. 4 similar curves are constructed for molar crown height in various stages of the *Elephas recki* specific lineage. Data for the earliest and latest phases of this presumed phyletic line are also included. Although the plotted samples are only approximately placed on the time scale according to their "average age" in dated deposits, the results here agree well with those for the suids.

Specimens from the *Mesoschoerus limnetes* zone give a mean indicated age of 2.5 m.y. with suggested limits of 3.4 and 2.1 m.y. Indicated ages and limits for the *Metridiochoerus andrewsi* and *Loxodonta africana* zones are 1.7 m.y. (2.1-1.4 m.y.) and 1.4 m.y. (1.7-1.2 m.y.). These last two figures are nearly identical to those obtained for the suids.

Taken together these data from elephants and suids may be combined to give a rough "best fit" age for the faunal zones including them. The ages are, of course, only approximate, but they are consistent with all faunal and geological evidence available at present (see Table 3).

The total span of time represented by the East Rudolf faunal succession includes more than three million years, from 4.5 m.y. to about 1.3 m.y. Within the sequence the oldest faunal zone (*Notochoerus capensis* zone) contains a fauna that correlates with assemblages from the Mursi and Kanapoi formations in other regions of the Lake Rudolf area; both these formations have been geophysically dated at about 4.0 m.y. old. The *Mesoschoerus limnetes* zone fauna correlates best with samples from the Shungura Formation succession between tuffs D and F. These tuffs are dated at 2.35 m.y. and 1.93 m.y. respectively¹⁵. The *Metridiochoerus andrewsi* zone fossils compare well with faunas from Olduvai Bed I and lower Bed II, both of which are younger than the 1.85 m.y. age obtained for the Basalt Member underlying them¹⁶. Correlates of the *Loxo-*

donta africana zone assemblage are not clear, but on the whole this fauna seems to be younger than lower Bed II at Olduvai and older than Bed IV. This could suggest an age close to that inferred above, that is about 1.3 m.y.

This faunal chronology at East Rudolf provides only a very tentative time scale against which the evolution of man and of other vertebrates can be studied, but within this framework the hominid fossils can now be listed by their level of occurrence (see Table 4) (specimen numbers and brief descriptions have already been published^{2,3}).

Table 4 Level of Occurrence of Hominid Specimens

Faunal zone	Lithostratigraphic units		<i>Australopithecus</i> KNM-ER number	<i>Homo</i>
	Ileret	Koobi Fora		
<i>Loxodonta africana</i>	Ileret Member	—	404, 725-29, 733, 739-41, 801-2, 806-9, 820, 805, 818-19, 993, 1170-71	731, 743, 803, 806-9, 820, 866-69, 992
<i>Metridiochoerus andrewsi</i>	Unnamed member	Upper member	403, 405-7, 732, 736, 738, 810, 812, 814-16, 997-8	164, 730, 734, 737, 742, 811, 813
<i>Mesoschoerus limnetes</i>	—	Lower member	—	414, 817

I am indebted to the many other workers who are conducting detailed research on the East Rudolf faunas for their discussions of unpublished data. These include H. B. S. Cooke (Suidae), S. C. Coryndon (Hippopotamidae), M. H. Day, J. F. Mungai, A. C. Walker and B. A. Wood (Hominidae), M. Beden (Proboscidae), J. Harris (Bovidae, Giraffidae and Rhinocerotidae) and M. and R. Leakey (Primates). Funds for this research have been provided by the National Geographic Society, Washington, DC. A grant from the Wenner-Gren Foundation for Anthropological Research, New York, supported my participation and the assistance of Mr A. B. Ricca in 1971. Mrs Kadgee Wilson prepared the figures for this report.

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Table 3 Age of Faunal Zones

	"Best fit" age m.y.	Indicated maximum m.y.	Indicated minimum m.y.
<i>Loxodonta africana</i> zone	1.3	1.6	1.0
<i>Metridiochoerus andrewsi</i> zone	1.7	1.9	1.5
<i>Mesoschoerus limnetes</i> zone	2.3	3.0	2.0

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Immunogenetic Model

JAN HIRSCHFELD

State Institute for Blood Group Serology, Statens rättskemiska laboratorium, Stockholm 60

Different and equally legitimate modes of interpreting serologic reactions will considerably change the image of reality. Some principles of such transformations are briefly outlined and applied to immunogenetic systems.

SEROLOGIC reactions are usually described with + and - symbols; their transformation into letter symbols can be accomplished in four different ways depending on whether the antibodies and/or antigens are regarded as monospecific or cross-reacting^{1,2}.

A monospecific (or simple) antibody contains only one hypothetical element called an "antibody specificity"²; a cross-reacting (or complex) antibody contains two or more of the specificities. Similarly, simple antigens have only one class of antigenic determinants and complex antigens have two or more.

Classes of Transformation

(1) In simple-simple models the basic antibodies and antigens defining the system are regarded as conceptually monospecific (simple). For instance, this is the case in the ABO-system of blood groups, in which only anti-A and anti-B are used and the A₁A₂ subgroups are not known.

(2) In simple-complex models the basic antibodies are regarded as simple (and consequently given a one-letter symbol). In this case, a haplotype can be "cross-reacting" (assigned two or more letter symbols). The Rh-system according to the notation of Fisher and Race is an example of these models.

(3) In complex-simple models the antibodies are regarded as conceptually but not necessarily operationally cross-reacting (complex). A given haplotype is regarded as having only one property (simple antigens), as in the Rh-system² and the Ag-system³.

(4) In complex-complex models antibodies and antigens can both be complex (assigned many letter symbols). Examples of this case are the Ag-system⁴ and the Rh-system described in this article.

Models that assume antibodies to be simple permit two antibodies to be identical (equal) or different (unequal). In contrast, complex-simple and complex-complex models permit two antibodies to be related in four different ways. They can be equal (anti-a and anti-a); not comparable and disjoint

Table 1 Set-theoretical Properties of Four Classes of Immunogenetic Models

Type of model	Relation between two Antibodies	Relation between two Antigens	No. of ants or antis Antibody	Antigen
(1) Simple-simple	ncd	ncd	1	1
(2) Simple-complex	ncd	(ncd), ncnd, cnd	1	Unlimited
(3) Complex-simple	ncd, ncnd, cnd	ncd	Unlimited	1
(4) Complex-complex	ncd, ncnd, cnd	(ncd), ncnd, cnd	Unlimited	Unlimited

ncd, not comparable, disjoint; ncnd, not comparable, not disjoint; cnd, comparable, not disjoint.

(anti-ab and anti-cd); not comparable and not disjoint (anti-ab and anti-ac); and comparable and not disjoint (anti-ab and anti-a). Similarly, simple-complex and complex-complex models permit the same four classes of "relatedness" between two antigens.

To describe in qualitative, discontinuous terms different degrees of "relatedness" between antibodies and antigens as well as the concept of serologic specificity the following hypothetical serologic units have been introduced⁵: antigenic specificity (ant); and antibody specificity (anti). An obligatory one-to-one relation exists between one ant and its corresponding anti. Simple antibodies and antigens have one and only one class of antis and ants, respectively, whereas complex antibodies and antigens contain two or more different classes of antis and ants.

In Table 1, some of the set-theoretical properties of the four

Table 2 T₃ Universe after Conventional Simple-Complex and New Complex-Simple Transformation

Reality (T ₃)	Simple-complex	Complex-simple
Haplotype (s)		
T(x)	ABCD	A
T(y)	ABEF	B
T(z)	ACEG	C
T(xy)	ABCDEF	D
T(xz)	ABCDEG	E
Reagent(s)		
Anti-xyz	Anti-A	Anti-ABCDE
Anti-xy	Anti-B	Anti-ABDE
Anti-xz	Anti-C	Anti-ACDE
Anti-x	Anti-D	Anti-ADE
Anti-yz	Anti-E	Anti-BCDE
Anti-y	Anti-F	Anti-BD
Anti-z	Anti-G	Anti-CE

Table 3 Restricted Binary Complex-Complex Model for Rh-system (axyzt Notation) at Nine Reagent/Eight Haplotype Level

Haplotypes	Anti-a (anti-D)	Anti-x (anti-CE)	Anti-y (anti-Ce)	Expected reactions with reagents Anti-z (anti-cE)	Anti-t (anti-ce)	Anti-xy (anti-C)	Anti-xz (anti-E)	Anti-zt (anti-c)	Anti-yt (anti-e)
Rh^{ax} (DCE)	+	+	—	—	—	+	+	—	—
Rh^{ay} (DCe)	+	—	+	—	—	+	—	—	+
Rh^{az} (DcE)	+	—	—	+	—	—	+	+	—
Rh^{at} (Dce)	+	—	—	—	+	—	—	+	+
Rh^{-x} (dCE)	—	+	—	—	—	+	+	—	—
Rh^{-y} (dCe)	—	—	+	—	—	+	—	—	+
Rh^{-z} (dcE)	—	—	—	+	—	—	+	+	—
Rh^{-t} (dce)	—	—	—	—	+	—	—	+	+

Fisher-Race notations are given within parentheses.

classes of immunogenetic models are given. Simple-complex and complex-simple models thus appear to give complementary descriptions, transformations or representations of a matrix of + and — signs distorting the interpretation of this matrix in opposite directions if antibodies and antigens in reality are assumed to be complex. In contrast a complex-complex model will be less distorting but too exhaustive and complicated if no restrictions are imposed. For example, a complex-complex model could be restricted by permitting a maximum of only two different antis and two ants in each antibody and antigen to define a particular immunogenetic system. This subclass of complex-complex models will be called "restricted binary complex-complex models" to distinguish them from other restricted models that permit more than two serologic units in each antibody and antigen.

The distortive effects of these various systems of description can be studied by the introduction and definition of hypothetical immunogenetic universes and by comparing their images after various transformations^{2,5}.

A T_3 universe contains three different species (x, y, z) of ants and antis as well as the simple genes T^x , T^y and T^z and has two chromosomal loci which may also contain one "silent" allele at each locus. An obligatory one-to-one relation exists between one gene and its corresponding ant, which in turn can react (combine) only with antibodies having the corresponding anti. Consequently, this T_3 universe can generate a maximum of three simple haplotypes (T(x), T(y) and T(z)), two complex haplotypes (T(xy) and T(xz)) and one "silent" haplotype (T(—)). In this universe, a maximum of seven different antibodies could exist representing the 2^3-1 different combinations of three antis (anti-x, anti-y and anti-z).

In Table 2, a T_3 universe is compared to the image of reality obtained after simple-complex and complex-simple transformation. It is interesting to note that the conventional (simple-complex) transformation gives a highly distorted image of the T_3 reality on the antigen side. Thus, despite the fact that the haplotypes T(x), T(y) and T(z) have no serologic property in common (except their ability to react with antibodies containing combinations of the corresponding antis), antigen T(x) receives two properties (A and B) shared with antigen T(y). A similar finding in an actual immunogenetic system could lead to protracted attempts in trying to isolate and characterize four different "antigenic determinants" in the simple antis T(x) and T(y).

The complex-simple model on the other hand depicts the simple antigens in a non-distortive way, but gives an erroneous image of the complex antigens T(xy) and T(xz), which according to their complex-simple notation (D and E respectively) appear unrelated. This apparent non-identity between T(xy) and T(xz) will also appear, for example, in absorption or immunodiffusion tests against reagents containing a separable mixture of anti-y and anti-z; if tested against an unseparable mixture of anti-y and anti-z (anti-yz), however, they will obviously give a reaction of identity^{4,6}.

The number of symbols in a T_3 universe are only three

(x, y, z). In a simple-complex model, seven symbols (A–G) are required and in a complex-simple model five symbols (A–E) are needed to account for the data generated by a T_3 universe after transformation.

In Table 3, a restricted binary complex-complex transformation of a T_3 universe (having two loci, simple genes and five different kinds of ants and antis) is given using a, x, y, z, t notation. The image of this universe after conventional simple-complex transformation using Fisher-Race D, C, E, d, c, e notation is also presented in this table.

The T_3 universe has at locus 1 the alleles T^a and T^- and at locus 2 the alleles T^x , T^y , T^z and T^t . After binary complex-complex transformation only simple and binary complex antibodies are permitted. The striking similarity of this T_3 universe with the Rh-system after simple-complex transformation makes it tempting to suggest that the Rh-system at the basic eight haplotype–nine reagent (8H–9R) level does in fact correspond closely to a T_3 system at a corresponding level of reality.

In principle the experimental and/or conceptual evidence for the new Rh model can be arranged into any of the four following classes: (1) Some or all reagents should be found to be at least conceptually cross-reacting (complex) and not mono-specific (simple) as implied by the conventional Fisher-Race and Wiener notations. (2) The reagents should be related to each other in identical or at least similar ways as postulated by the model. Thus anti-c (anti-zt) should at least be conceptually regarded as a mixture of anti-cE (anti-z) and anti-ce (anti-t). (3) It should be shown that for example the E antigens (x and z) in the haplotypes CdE (Rh(x)) and cdE (Rh(z)) are at least not identical and preferably completely unrelated except for their ability to react with reagents containing mixtures of anti-x and anti-z (e.g. "anti-E" which in the model is anti-xz), or "anti-DE" (anti-axz). (4) Certain other data, which according to a conventional simple-complex model require more or less complicated additional assumptions, should be easily explainable and "understood" or even "trivial" in the conceptual image formation given by the new model. In the latter case, the "triviality" of certain data occurs only after the model has been generally accepted. Before that stage, such "trivial" data are of great interest in demonstrating the "predictive power" or serving as a "verification" of the model.

Experimental evidence supporting the new Rh-model has been given elsewhere⁷. The importance in general serology and immunology of the "new serology" which has been briefly outlined and summarized here should be obvious.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Black Holes and Temporal Ordering

THE "Arrow of Time" has been much discussed by philosophers and by some scientists¹, and various manifestations, which have also been offered as explanations of this directionality, are to be noted in the world around us. For example, asymmetry of time is observed in thermodynamics, an increase in entropy is predicted from statistical mechanics, there is a consistent choice of retarded solutions to time symmetric equations of radiation theory and expansion of the universe is deduced from cosmological theory; in addition a temporal arrow is inferred from the asymmetry of matter and antimatter in the universe. A striking feature of such observations is that the directions of the arrows agree.

Within general relativity it is necessary to impose time orientability on the E_4 manifold such that the arrows placed on timelike world lines agree in sign. Thus an assumption is made concerning temporal asymmetry which may not be derivable within the context of general relativity.

A theory purporting to explain "Time's arrow"² generally involves a plausibility argument concerning one of these arrows within a system which is in contact with its complement, the remainder of the universe. The universe is supposed to act as an infinite sink for the dissipation of energy from the system, and, as a result of the interaction or interdependence of all systems and processes, it is concluded that all of the manifestations of temporal asymmetry within the universe agree on direction.

A consequence of this argument is that within a system isolated from the remainder of the universe, asymmetry of temporal order may not be maintained; in other words, the system will reach a state of dynamical equilibrium. To some extent a Black Hole provides such a situation, since world lines and radiation may not escape from a system which has fallen through its Schwarzschild radius³. It is, however, possible for exterior particles and radiation to enter the hole, and some of its rotational energy may be extracted from the ergosphere⁴.

The Wheeler-Feynman absorber theory of radiation⁴ offers an explanation for the appearance of retarded radiation, resulting from initially time symmetric solutions to Maxwell's equations, by establishing a connexion with the thermodynamic properties of matter in the universe. Within a Black Hole, however, while retarded signals converge towards the origin of the singularity, it is possible for advanced signals to escape along past pointing null cones. Within the Wheeler-Feynman explanation one would be faced with the possibility of the reversal of temporal direction inside the hole and the emission of advanced radiation.

Thermodynamic arguments within a Black Hole require an unambiguous meaning to be given to the notion of entropy within the hole. It would appear, however, that dissipative processes with the attendant spontaneous increase in "disorder" are not possible within the Hole.

It therefore seems reasonable to question the assumption of a fixed temporal direction for the collapse of a Black Hole and the issue of the final state. Indeed, one may go

further and question the meaning of the terms "time" or "proper time" as applied to processes within the Black Hole since, as a result of the bending of light cones towards the origin, it is not generally possible to construct a "clock" in which retarded signals are exchanged between two world lines inside the hole. Thus the nature of temporal flow in regions of pathological geometry is ambiguous.

My object here is to draw attention to one of those classical assumptions as to the nature of time which has remained unexamined in the light of quantum physics and general relativity, and to stimulate discussion directed towards clarification of these matters.

F. D. PEAT

National Research Council of Canada,
Sussex Drive, Ottawa, Ontario K1A 0R6

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Is the African Plate Stationary?

THE islands of St Helena, Tristan da Cunha and Gough lie respectively 500 km, 450 km and 450 km east of the crest of the Mid-Atlantic Ridge¹ (Fig. 1). We believe that they overlie hot spots or convective plumes in the mantle and that the Walvis Ridge is the trail of a hot spot marking the relative motion of the African plate over the mantle since the opening of the South Atlantic^{2,3}. We suggest that the termination of the ridge at Tristan and Gough records the cessation of this relative motion. That this occurred about 25 m.y. ago is indicated by a spreading rate of 1.7 cm/yr/side and because the two islands lie just east of magnetic anomaly six⁴. Spreading of the sea floor continued and has moved the crest west from the hot spots. The Discovery and Meteor seamount chains are concentric with the Walvis Ridge; they too terminate some distance east of the crest of the Mid-Atlantic Ridge and may also be hot spot trails terminating on the same isochron. The position of Bouvet Island is harder to interpret because of its location at the western end of the Atlantic-Indian Ridge.

On the other side of the African plate, Mauritius and Reunion (200 km apart) also lie on anomaly six at the end of a ridge concentric with the Walvis Ridge⁵ which suggests that they also overlie a plume. At the same time that relative motion between the African plate and mantle ceased (25 m.y. ago) the pattern of spreading in the Indian Ocean altered and what had been the Chagos Fracture Zone became the crest of a new Central Indian Ridge⁵. Its subsequent spreading has created young ocean floor east of Mauritius.

Stratigraphic evidence and K/Ar dates from widely separated areas on the African plate indicate a roughly simultaneous upsurge in volcanic activity about 25 m.y. ago (Table 1). If this volcanism was generated over plumes and the African plate has moved laterally over them during the past 25 m.y., then the volcanoes should form parallel lines across Africa.

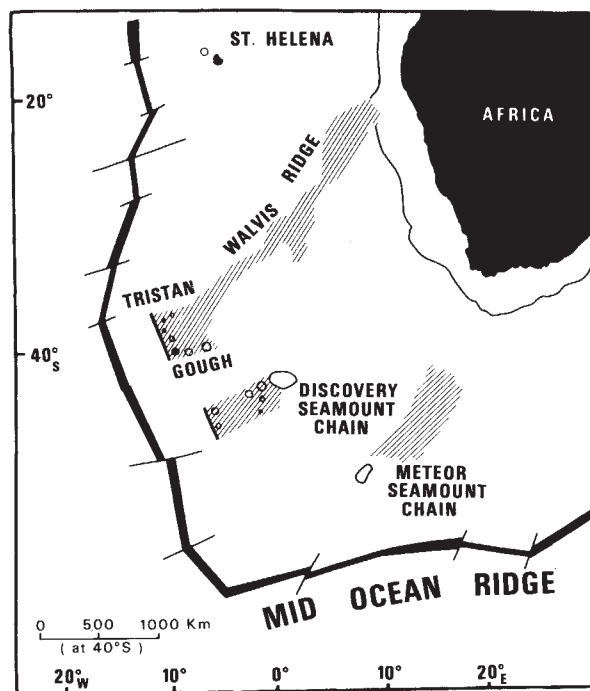


Fig. 1 St Helena, Tristan, Gough, and the ends of the Discovery and Meteor seamount chains lie some hundreds of km east of the crest of the Mid-Atlantic ridge. This could be the result of relative motion between the African plate and hot spots stopping about 25 m.y. ago.

If the motion averaged 1 cm/yr the lines of volcanoes would be 250 km long and all would become younger in the same direction. Fig. 2 and Table 1 indicate that although African Neogene volcanoes are commonly arranged in lines the lines are not parallel and there is no evidence of consistent age variations from one end to another. This pattern of volcanism is consistent with the hypothesis that the African plate halted and has been virtually at rest for the past 25 m.y. with each Neogene volcanic area overlying a different plume.

Before the acceptance of plate displacement it seemed appropriate to relate surface structures directly to those of the underlying asthenosphere but this is no longer realistic unless a plate can be shown to be temporarily at rest.

Krenkel⁶ was the first to draw attention to the basin and swell structure (Fig. 2) which is peculiar to Africa, and Cloos⁷ linked these structures to rift valley formation. Burke and Whiteman⁸ have postulated a genetic sequence, discernible in Africa, from uplift, through rifting and triple junction formation to continental separation. We suggest that these peculiarities of Neogene African structure (in no other continent are they so prominent) may be a consequence of the standstill of the African plate over the asthenosphere.

Fig. 2 is a sketch of the Neogene volcanoes, basins and swells of Africa and these features may reflect the structure below the bottom of the lithosphere. The basins and swells shown in the figure (which are generalized from topographic maps) have wavelengths of about 2,000 km and amplitudes of about 1 km. Smaller scale uplifts about 1 km high average about 100 km across and 200 km in length⁸. These smaller scale features are associated with major negative gravity anomalies and lines of volcanoes which show no consistent ageing pattern (Table 1).

Nine volcano crested uplifts are tangentially disposed about the Chad basin and another eight or nine arranged in a straight line form the Cameroun Zone, half on the continent and half in the ocean. The Eastern and Western rifts are marked along their lengths by local uplifts of the same scale and the rifts themselves show a rude tangential disposition

Table 1 Neogene Volcanism on the African Plate

Volcanic group	Approximate length (km)	Approximate azimuth (degrees)	Age range	Ref. No.
Tristan	—	—	18 m.y. to Recent	27
Gough	—	—	20–25 m.y. to Recent	28
Cape Verde	300	Circular	6 m.y. to 2 m.y.	27
Madeira	50	110	Mio-Pliocene to Recent	29
St Helena	—	—	Cenozoic	—
Canary Islands offshore	300	110	14 m.y. to 7 m.y.	33, 34
Canary Islands inshore	250	45	22 m.y. to Recent	30
Dakar	50	—	22 m.y. to Recent	30
Air	100	—	Miocene (?) to Lr Pleistocene	31
Edgere, Hoggar	60	45	Cenozoic	32
Ajjar, Hoggar	100	75	Cenozoic	32
Atakor and Anahef, Hoggar	250	45	Cenozoic	32
Jos	100	135	Cenozoic	32
Benue	500	45	Pliocene to Recent	35
Biu	80	125	22 m.y. to Recent	35
Cameroun Zone (8 uplifts)	1,100	30	5 m.y. to Recent	35
Tibesti	400	120	25 m.y. to Recent	35
Haruj	400	120?	Post-Eocene to Recent	36
Jebel Marra	200	0	Pliocene to Recent	37
SE Uganda older group	60	10	Tertiary to Recent	38
E Uganda younger group	300	0	30 to 25 m.y.	39
Kavirondo rift	200	60	22 to 12.5 m.y.	39
Kenya rift	800	0	22 to 2 m.y.	39
Ethiopian rift	400	50	Miocene to Recent	40
			Eocene to Recent, mainly less than 25 m.y.	41
Rungwe	80	140	Pliocene to Recent	42
Comores	200	120	? Miocene to Recent	43
Mauritius	60	30	12 m.y. to Pleistocene	44
Reunion	75	130	Pleistocene	45

Although the volcanoes are arranged in lines these lines have no consistent trend nor do they get younger in any one direction. Where age data are available they show that the volcanism either started or became greatly intensified at the beginning of the Miocene about 25 m.y. ago. Volcanoes at plate margins are omitted.

within the East African Swell. It appears that structures of two orders of magnitude, the smaller with a marked horizontal asymmetry, may be making their presence felt through the African plate.

There appear to be systematic differences between various parts of the continent which may reflect differences deep in the mantle. Higher ground is concentrated to the east and south of the Congo basin and there is no Neogene volcanism south of that basin. Rifting is restricted to the north-east and Bouguer anomalies are about 60 mgal lower in the centre of the continent than in the north⁹. Earthquakes are closely linked to the rift system although a line of epicentres extends south down the axis of the continent¹⁰.

Although the present phase of uplift, volcanism, rifting and continental break-up began in Africa only about 25 m.y. ago, earlier activity between 100 and 200 m.y. ago when Gondwanaland broke up was similar^{8,11}. The absence of a consistent ageing pattern along lines of African Mesozoic intrusives may also record a former standstill. If this is generally true fossil rifts and aulacogens up to 2,000 m.y. old may record local plate standstills as far back as the beginning of the plate tectonic regime¹². Because oceanic lithosphere is only two-thirds as thick as continental lithosphere¹³ more volcanoes related to plumes may form in ocean basins except in the case of stationary continents.

We relate most if not all volcanoes to plate boundaries or to plumes because of evidence in Hawaii and because there are at

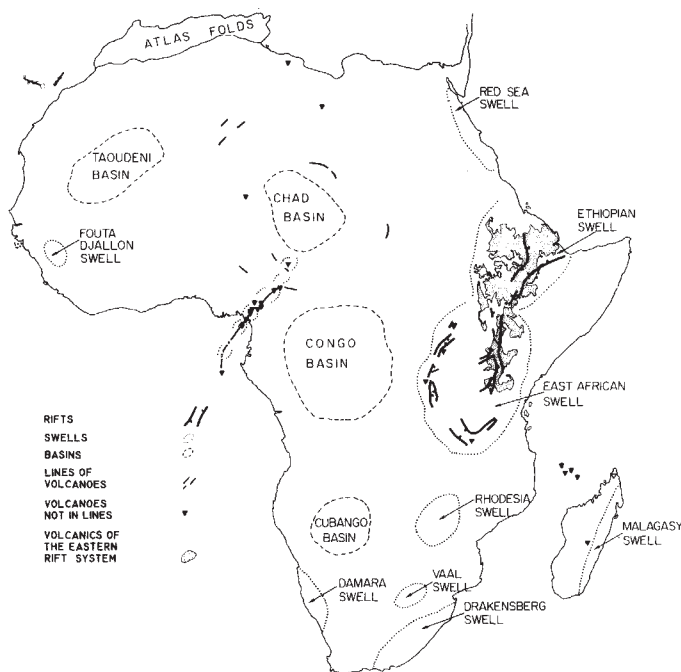


Fig. 2 Neogene basins, swells, volcanic uplifts and lines of volcanoes on the African plate. The lines are not concentric and do not get younger in consistent directions. This can be interpreted as indicating that the African plate is at rest over the deep mantle.

least two indications that African Neogene magmas originate from below the lithosphere. First, the continental lithosphere is about 110 km thick and the alkali basaltic composition which characterizes most African Neogene volcanism requires partial melting at this or greater depths¹⁴. Second, the huge volume of material in the Neogene volcanics of East Africa (600,000 km³) would be hard to derive from within a 110 km thick lithosphere¹⁵.

The accumulated data suggest that the rise of swells in Africa may be due to convection plumes in the mantle which by lifting parts of the continent have resisted and halted eastward motion from the Mid-Atlantic Ridge and have held Africa stationary for about the past 25 m.y. Meanwhile sea floor spreading has caused the crest of the Mid-Atlantic Ridge in the South Atlantic to move westwards, off the plumes which originated it. The implication that fresh plumes rising under continents are more vigorous than older plumes in oceans may also explain why mid-ocean spreading rates slow down as oceans broaden. If Africa halted with only a minor contemporary change in the Atlantic spreading rate¹⁶, the rate of rotation of the Americas plate westward over the mantle must have doubled about 25 m.y. ago.

Dott¹⁷ noted many examples of tectonic changes around the Pacific at that time. Jackson *et al.* hold that the Hawaiian-Emperor Chain is the trail formed over a persistent melting spot or plume in the mantle¹⁸ and ascribe the sharp bend in the chain to a sudden increase 24.6 ± 2.5 m.y. ago in the westward component of motion of the Pacific plate to a rate of 14.8 cm/yr in a direction west-north-west. Others favour a somewhat slower rate¹⁹. The East Pacific Rise at the corresponding position of about 10° S has a total spreading rate of 12 cm/yr, suggesting that the crest of East Pacific Rise is moving westwards over the mantle at 8.8 cm/yr or less. If stationary plumes underlie Galapagos and Easter Islands this could explain why these islands now lie east of the crest, although their separation from the crest seems to be rather small. Also the Nasca plate should be moving westward at 2.8 cm/yr or less and may be nearly stationary. Perhaps the acceleration of the Americas plate halted it, in spite of the intervening subduction zone.

Molnar and Sykes²⁰ note only "a minor belt of activity" between the Nasca and Caribbean plates near Panama so that the latter may also be nearly stationary.

Relative to Africa, Eurasia is rotating southwards about poles at 9° N, 46° W and 9° S, 134° E²¹. The second is at the eastern end of Indonesia and any part of the Eurasian plate over it would be stationary relative to Africa. A series of faults crossing China from Burma to Korea give indications of left hand motion implying that the China plain is rotating southward less rapidly than the rest of Eurasia. Thus much of China and all of South-east Asia between the Indian Ocean and Philippine Sea may be halted. As in Africa, China has much volcanism that started in mid-Tertiary time and the Ordos Plateau appears to be a dome which is rising rapidly with a rift valley system around it from Sian through Taiyuan to Peking (ref. 22 and personal communication from Chinese scientists). Another seismic line extending from the Pamirs to past Lake Baikal may mean that Sinkiang, Mongolia and the Lake Baikal rifts are moving only slowly over the mantle, again like Africa.

If these absolute motions over the mantle are approximately correct it is possible to generalize that circular island arcs have formed where ocean floors are advancing over the mantle towards the convex sides and continents are retreating from or stationary behind their concave sides (North-east Asia, Aleutian, West Indian and Scotia arcs and Indonesia from the Andaman to Java Seas). On the other hand, arcs have not formed off coasts which are advancing over the mantle and ocean floor which is nearly stationary over it (Chile-Peru and Mindanao).

The orocline concept²³ is incompatible with strong plates and offers no reason why arcs should be circular. Frank's explanation²⁴ might be expected to apply where an oceanic plate is advancing over the mantle and free to shape its own subduction zone but not where a continent is advancing over the mantle and overriding the zone. Plafker²⁵ supports this interpretation for the Aleutians, but is uncertain about the motion in Chile although recognizing great structural differences.

It should be noted that two ridges, the South Atlantic Ridge and East Pacific Rise, seem to have spread smoothly about crests and poles stationary relative to the mantle throughout later Mesozoic and Palaeogene time.

The South Atlantic and Pacific oceans could expand without interfering with one another because subduction zones around the Pacific separated them but they would have interfered with the development of other oceans not so separated from them. For example, if the pole for spreading between Africa and the Americas was fixed near Greenland, the Americas and Eurasian plates, their rotation pole, now near New Siberian Islands, and the Arctic spreading ridge, must all have been moving over the mantle. This could explain why the spreading axis of the Arctic Sea has jumped to a new location at about 20 m.y. intervals²⁶ and similar arguments could explain the complex patterns of the Northern Atlantic and Indian Oceans and Tasman Sea.

Plumes seem to have average lives of the order of 100 m.y. Competition between vigorous fresh plumes and older ones appears to be the major cause of plate motion and of its changing patterns and rates, and hence the mainspring of geological history.

K. BURKE
J. T. WILSON

Erindale College,
University of Toronto,
3359, Mississauga Road, Clarkson,
Ontario

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Glaciation in the Somerset Levels: the Evidence of the Burtle Beds

KELLAWAY has postulated¹ an ice stream of Wolstonian (Saale) age moving from the Bristol Channel, across the lowlands of Somerset and into Wiltshire. He suggested that erratic rocks, including the "bluestones" from the Prescelly Hills of Pem-

brokeshire, subsequently erected in the Stonehenge monument, were carried into the chalk upland by this, or the earlier Anglian, ice sheet. At least one piece of the evidence he cites to support this hypothesis can be subjected immediately to critical examination. Kellaway described the Burtle Beds of Somerset in the following terms: "Other residual masses of glacial sand and gravel ('Burtle Beds') rise out of the marshes at Catcott Burtle, Weston Zoyland and Othery". Their marine origin is cursorily dismissed in the phrase "These outwash deposits, previously thought of as marine. . .". These deposits have, in fact, recently been the subject of detailed re-investigation^{2,3}. This new work supports the conclusion by Bulleid and Jackson^{4,5} that the sands and gravels of the Burtle Beds are of marine origin. If that is the case then Kellaway's "glacial" hypothesis is much weakened. It is, therefore, important to review the grounds for re-asserting the marine character of the Burtle Beds.

The Burtle Beds are confined to the valleys of the Rivers Brue, Parrett and Tone. Although the Kenn gravels⁶ and the "marine Pleistocene" deposits in the Vale of Gordano⁷ have been tentatively correlated with the Burtle Beds, this correlation has not been confirmed. Hawkins and Kellaway⁸ conclude that the Kenn gravels are of glacial origin but do not give their detailed evidence. The distribution of the Burtle Beds proper (Fig. 1) is precisely that which would be expected to result from a marine incursion into the Somerset Levels. The known Holocene marine sands conform to a similar pattern if lower sea levels are taken into account. In no case are the Burtle sands and gravels found on the interfluvies above the 50 foot contour, as could be expected if they were of glacial or fluvio-glacial origin. Their characteristic surface form reminds us of the sandbanks in the present Parrett estuary. So striking is the similarity that a comparison on both petrological and faunistic grounds seems desirable. Dr M. R. Dobson, of the Geology Department of the University College of Wales, compared the Burtle gravels with those from various locations in the estuary. He found that they are indistinguishable on petrological grounds. Dr J. D. Fish, of the Zoology Department, examined a collection of marine shells from the Burtle Beds and agreed with Prestwich's⁹ original conclusion that they represent a fauna similar to that now inhabiting the British seas. It is pertinent to repeat Prestwich's assessment that "There is a marked absence of such northern shells as *Astarte borealis*, *Leda permula*, *Fusus islandica*, *Natica groenlandica* and others common in the Glacial drifts".

The upper surface of the Burtle sand and gravel deposits has clearly been subjected to non-marine erosion. The absence of surface cryoturbation phenomena, in spite of some evidence of solifluction, suggests that this erosion was dominantly fluvial rather than glacial or periglacial. The deposits give the appearance of having been dissected by streams flowing to the Parrett and Brue. This dissection has not disturbed the structures within the Burtle Beds which make it impossible to accept a glacial origin. Everywhere within the area south of the Mendips, the deposits are horizontally or nearly horizontally bedded. Shell layers, most often composed mainly of *Macoma baltica*, are almost totally undisturbed. A high proportion of the bivalves are still articulated. Occasionally locations are found where forms common on rocky shores occur in great numbers. A general picture emerges of a range of habitats comparable to that of the present estuary and without any of the signs of re-sorting and re-distribution which a glacial or fluvio-glacial disturbance would cause.

There are, however, much more substantial grounds for concluding that they are undisturbed marine deposits. A series of boreholes has been sunk through the Burtle Beds (Fig. 1 shows the locations at Catcott Burtle, Brickyard Farm and Cutley). The results are given in Fig. 2. The sands and gravels of the Burtle Beds are shown to rest conformably on clays of similar age, the microfaunas of which indicate a progressive marine transgression.

We examined ten selected samples from four of the boreholes

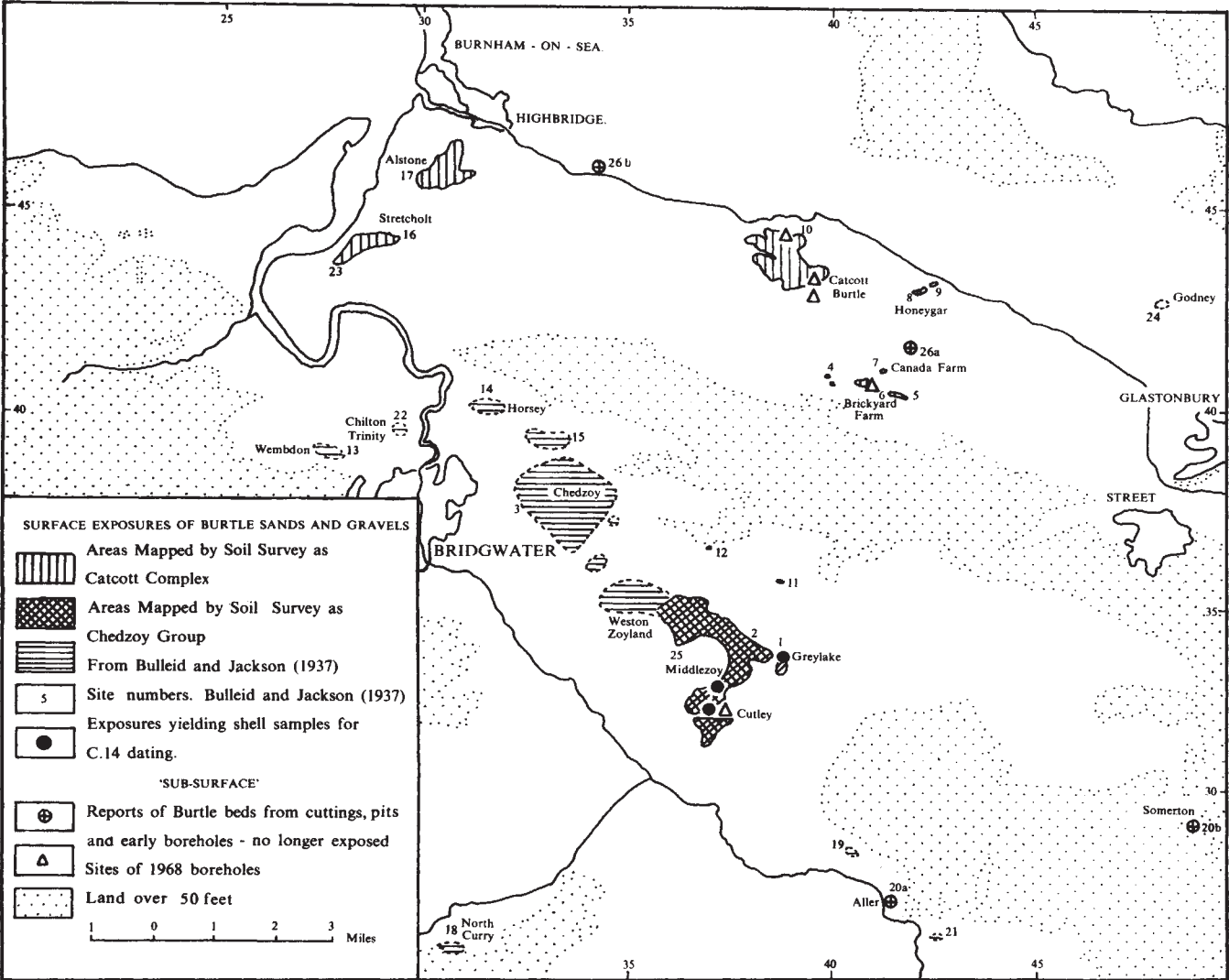


Fig. 1 The Burtle Beds of Somerset.

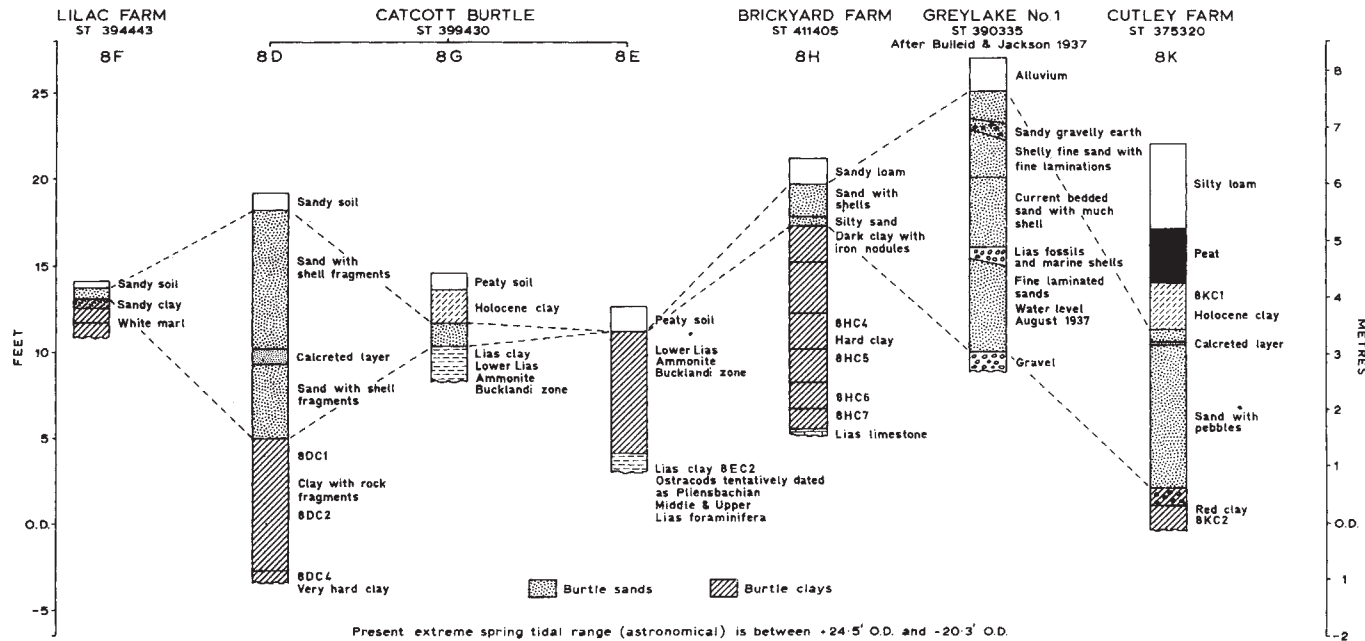


Fig. 2 Boreholes through the Burtle Beds.

FAUNA		SAMPLES										
QUATERNARY (?EEMIAN) MICROFAUNA	FORAMINIFERA		AMMONIA BATAVUS A. BATAVUS VAR. A. LIMNETES A. TEPIDA A. SPECIES ASTERIGERINATA MAMILLA BOLIVINA PSEUDOPPLICATA BULIMINA ELONGATA B. GIBBA B. MARGINATA CIBICIDES FLETCHERI C. LOBATULUS C. REFULGENS C. SPECIES ELPHIDIUM c.f. ADVENUM E. CLAVATUM E. CRISPUM E. SELSEYENSE E. WADDENSIS E. WILLIAMSONI E. SPECIES GLOBULINA GIBBA LENTICULINA SUBORBICULARIS NONION POMPILOIDES PATELLINA CORRUGATA PLANORBULINA DISTOMA PROTEPHIDIUM ANGLICUM QUINQUELOCULINA LATA ROSALINA ANOMALA R. PRÆGERI R. WILLIAMSONI TRIFARINA ANGULOSA	8DC4	8DC2	8DC1	8EC2	8HC7	8HC6	8HC5	8HC4	8KC1
	OSTRACODS				•	•	○			○	○	○
LIAS MICROFAUNA (DERIVED)	FORAMINIFERA		CYPRIDEIS TOROSA CYTHOPTERON NODOSUM HEMICYTHERE ANGULATA HIRSCHMANNIA VIRIDIS LEPTOCYTHERE PELLUCIDA LOXOCOCHA ELLIPTICA AMMODISCUS SPECIES ASTACOLUS S. DENTALINA S. FRONDIOLARIA S. LENTICULINA S. LINGULINA S. MARGINULINA S. NODOSARIA S. PLANULARIA S. VAGINULINA S. BAIRDIA MOLESTA HUNGARELLA SPECIES PROCYTHERIDEA S. LOPHODENTINA S. LOXOCOCHA ELLIPTICA	8DC4	8DC2	8DC1	8EC2	8HC7	8HC6	8HC5	8HC4	8KC1
	OSTRACODS				✓	✓	✓	✓	✓	✓	✓	✓
Symbols showing numbers in 50 gms stand. weight.			• = 1 ○ = 2-5 ○ = 6-20	• = 21-50 ○ = 50+	• = present							

Fig. 3 Microfauna in selected samples from Burtle clays.

from the Flandrian and Recent of Great Britain and also occur in the last interglacial (Eemian) of Shortalstown, Rosslare¹⁰ and Selsey¹¹. There are no cold water species.

The Quaternary microfauna is of low diversity and dominated by *Ammonia* species. This is consistent with estuarine accumulation. The absence of high marsh agglutinating species and fewness of low marsh calcareous species support the idea of depths below low tide mark. The high marine forms such as *C. lobatulus* and *E. crispum* can be accounted for as swept in contemporaneously by currents from the Bristol Channel. The associated microfauna apart from the foraminifera and ostracods (not shown in Fig. 3) also contains a mixture of strong, estuarine elements such as *Hydrobia* species with swept-in fragments of marine forms including bryozoans, sponge spicules and echinoid spines (known to occur as far up as the tidal limit of the Severn today and a feature of Flandrian estuarine faunas in the area).

In short, the evidence of the microfauna strongly supports the idea of accumulation in place and lends no credence to the idea of glacial transport.

All the evidence cited above from the boreholes, which were sunk specifically to examine the Burtle Beds, testifies to the estuarine and marine origins of the Burtle sands, gravels and clays and to their accumulation in place. There is no contrary evidence from the large number of boreholes sunk by contractors for the M5 motorway (Soil Mechanics, Ltd). This line of boreholes does not cross any of the major Burtle Bed outcrops. Except on the flanks of Puriton Hill, in-place Burtle deposits are not encountered. Some of the boreholes do pass through a few feet of sand which has been interpreted by the present authors either as blown sand or as derived from the Burtle Beds. In many of these boreholes the sand lies above a peat layer dated by ¹⁴C as roughly 8000 BP (I 4402 8480 ± 140 BP and I 4403 8360 ± 140 BP) and is therefore much more recent than the Burtle Beds. In those boreholes where the 8000 BP peat is not encountered, the similarity of the sands to those in the boreholes where the peat layer is present strongly suggests a similar age and origins. The rarity of shells, the absence of calcareous layers and the uncemented character of the sands all support this.

The surface form, the internal structure and the character of both the surface sediments themselves, and their included marine micro and macro-faunas, thus all imply an estuarine or marine origin modified only by subsequent sub-aerial denudation. We believe that any suggestion that the Burtle Beds are ice transported is quite untenable. A fluvio-glacial origin is, in our opinion, so unlikely as to be unacceptable, even on superficial characteristics.

C. KIDSON
J. R. HAYNES

Department of Geography,
University College of Wales

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for microfauna (Fig. 3). These samples were taken from the clays immediately above the unconformity with the Lias and at higher horizons, including one between the sands (8KCI).

Our principal conclusions, drawn from the analysis of the microfossils found in 50 g of original sample washed through a 100 sieve (Brit. Stand. 150 µm), are as follows.

The microfauna, considered as a whole, includes 32 species of foraminifera and 6 species of ostracods of Quaternary age with 10 species of foraminifera and 5 species of ostracods reworked from the Lias. No other time periods are represented.

The Lias contaminants are most abundant in the samples immediately above the contact and decrease upwards. There are none in the highest samples examined from D, H and K. The fauna above the contact in E is exclusively Liassic. This would be expected if the beds are in place and represent a progressive marine transgression but unlikely in glacially transported strata. Nor is it necessary to postulate a distant origin for these forms which can be accounted for by local reworking and downwash.

The Quaternary microfauna includes forms that are known

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Distribution of Cadmium in North Atlantic Deep-Sea Sediments

THERE is little information available on the concentration of the volatile, biologically toxic, element cadmium in deep-sea sediments. We present here some data on its distribution in a series of North Atlantic deep-sea sediments.

The material analysed, which included associated sea salt, was taken from the top portions of various NAVADO¹ cores, and Cd was determined on a dithizone extract of a digest of the sample using an atomic absorption carbon rod atomization technique. Sampling locations and the Cd contents of the cores are given in Table 1. The more important findings are,

Table 1 Sampling Location and Analytical Data from North Atlantic Deep-Sea Sediments

Core	Location	Total carbonate content (wt. %)	Cd content (p.p.b.)	
			Total sediment	Carbonate-free basis
C 2	16° 02' N, 29° 43' W	54	120	260
E 3	22° 04' N, 35° 34' W	1	40	40
E 6	21° 48' N, 56° 41' W	1	40	40
E 7	22° 06' N, 69° 05' W	5	275	290
F 1	25° 06' N, 70° 22' W	12	315	360
F 3	25° 12' N, 57° 24' W	10	200	220
F 4*	24° 55' N, 49° 15' W	58	300	710
F 5*	24° 49' N, 39° 28' W	77	215	935
F 7	25° 11' N, 19° 44' W	66	315	925
G 3*	27° 41' N, 49° 10' W	51	295	600
G 4	27° 49' N, 65° 54' W	2	490	495
H 6	30° 53' N, 23° 08' W	63	190	515
I 1	33° 52' N, 12° 56' W	59	285	695
J 2	36° 39' N, 63° 10' W	42	250	435
J 3	37° 46' N, 55° 00' W	32	305	450
J 4*	37° 27' N, 38° 00' W	89	115	1,035
J 5*	37° 15' N, 27° 40' W	74	230	885
K 6	39° 14' N, 69° 19' W	35	95	145
L 4*	43° 03' N, 23° 16' W	55	300	665
L 5*	43° 01' N, 17° 14' W	88	150	1,230
M 3*	45° 59' N, 32° 11' W	45	250	455
N 1	49° 10' N, 41° 32' W	13	100	115
N 2*	48° 52' N, 34° 12' W	32	580	850
N 3*	48° 40' N, 24° 31' W	20	370	460
N 4	48° 55' N, 17° 12' W	60	265	660
O 2	52° 00' N, 17° 50' W	13	190	220
P 2	55° 09' N, 22° 45' W	49	190	380
P 3*	55° 56' N, 35° 30' W	45	300	545
Q 1	57° 59' N, 10° 04' W	44	40	70
Q 3*	57° 56' N, 29° 08' W	57	220	510
R 2	60° 54' N, 13° 05' W	50	40	80
R 3*	60° 58' N, 20° 58' W	26	145	195
R 4*	61° 04' N, 32° 30' W	32	320	470
S 3*	64° 02' N, 28° 57' W	5	190	200
T 3	68° 36' N, 06° 55' W	36	200	310
Average; all deep-sea sediments				225
Average; deep-sea clays (<30% total carbonate)				215
Average; deep-sea carbonates (>30% total carbonate)				235

* Sediments from the Mid-Atlantic Ridge and ridge flank system.

first, the average Cd content of the North Atlantic deep-sea sediments analysed is 225 p.p.b. (p.p.10⁹). This is close to the average of 271 p.p.b. Cd given for two deep-sea sediments from the North Atlantic². Second, the average Cd content of our samples containing >30% total carbonate is 235 p.p.b., compared to 215 p.p.b. for samples containing <30% total carbonate; there is little difference, on average, between the Cd contents of sediments containing a large proportion of carbonate shell material and those consisting predominantly of lithogenous components.

We have suggested³ that because deep-sea carbonates and deep-sea clays contained similar amounts of Hg it was incorrect to use calculated carbonate-free values to assess geographical trends in the distribution of this element. Subsequent analyses showed that the relatively high Hg content of carbonate shell material justified this approach. To investigate further the

association between Cd and carbonate material a number of shells were separated from 12 of the deep-sea sediments; the range of Cd contents in the shells was <5 to 120 p.p.b., with an average of 55 p.p.b. Our material consisted predominantly of the shells of foraminifera, and the average of 55 p.p.b. Cd may be compared with that of 28 p.p.b. found in the shells of near-shore marine organisms². It is apparent, therefore, that although some carbonate shell can contain ~100 p.p.b. Cd, shell debris in general acts as a diluent on the Cd present in non-carbonate components, such as the clay minerals.

Third, both in the total sediment samples, and on a calculated carbonate-free basis, there is a tendency for higher Cd contents to be found in mid-ocean areas. For example, the average carbonate-free Cd content for these samples from the Mid-Atlantic Ridge and ridge flank system (see Table 1) is 650 p.p.b., compared to 335 p.p.b. for sediments from other localities. Sediments from the mid-ocean ridge system contain, on average, more total carbonate than those from other localities. The average Cd content of shell material from ridge samples (55 p.p.b.) is the same as that from non-ridge samples (55 p.p.b.), and if allowance is made for carbonate-associated Cd it is apparent that the non-carbonate fractions of mid-oceanic ridge sediments are significantly richer in Cd than those from other Atlantic deep-sea localities.

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S. R. ASTON
R. CHESTER
A. GRIFFITHS
J. P. RILEY

*Department of Oceanography,
The University,
Liverpool L69 3BX*

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Cathodoluminescence in Deformed Diamond

WE describe here, for the first time, changes in the cathodoluminescence of diamond, caused by deformation. Fig. 1—a scanning electron micrograph—shows part of a polished (100) surface of a diamond. This surface had been prepared for another experiment by polishing in the [001] direction with 0–1 µm powder, and then in the [010] direction with a nominal 4–8 µm powder. The surface damage shown in Fig. 1 appeared during polishing with the coarser powder. The area is approximately square in outline with sides about 30 µm long, but two of the four sides appear fore-shortened, as the surface was tilted in the microscope to bring out detail. The damage is similar to the ring cracks produced on diamond surfaces by loading them with a ballbearing. An analysis of these ring cracks^{1,2} shows that the damage consists primarily of a cone crack, spreading outward and downward from the surface, which is held open by debris when the load is removed. The stone is thus left in a state of elastic strain, particularly in the region within the surface crack.

We also viewed the same surface in the cathodoluminescence mode of the scanning microscope, by observing photon emission from the diamond. This particular diamond (unlike many



Fig. 1 Scanning electron micrograph of part of a polished diamond surface, approximately 30 μm square.

others) shows very little variation in the intensity of cathodoluminescence over the surface, except near two ring cracks and another area of surface damage of similar size. Fig. 2 shows the same view of the surface shown in Fig. 1, but taken in the cathodoluminescence mode. The cracked areas in Fig. 1 are delineated by the cathodoluminescence, but in addition the intensity of the emitted light is much reduced over a large area within the ring, where the print appears dark. Very similar effects are observed at the other ring crack. A comparison of Figs. 1 and 2 also shows that the cathodoluminescence is reduced in the neighbourhood of some of the polishing lines.

The nature of ring cracks in diamond, outlined above, suggests two mechanisms by which the cathodoluminescence could be affected by damage. The presence of cracks under the surface may give rise to internal reflexions which prevent emitted light from leaving the crystal. Alternatively the elastic strain due to unhealed cracks might alter the emission conditions. The fact that the dark area is within the ring where the elastic strain is greatest, rather than outside the ring where the cone crack spreads out and down, tends to favour the second hypothesis. We are at present making further experiments to investigate the effect of elastic strain. It is, however, already clear that cathodoluminescence permits a rapid method of detecting mechanical damage in diamond, otherwise not readily visible.

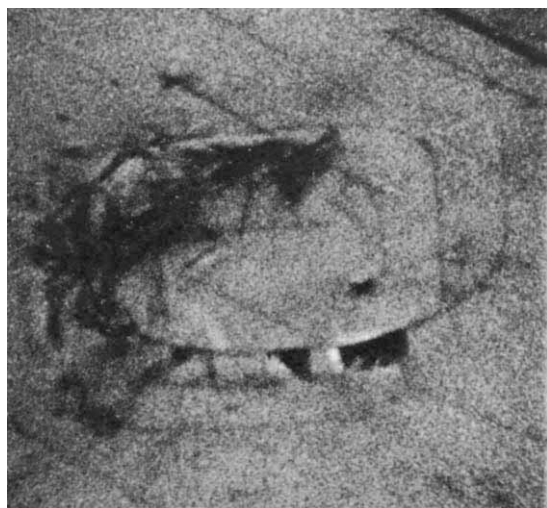


Fig. 2 The same area viewed in the cathodoluminescence mode off the microscope.

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M. CASEY

J. WILKS

Clarendon Laboratory, Oxford

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Laser Analogue to Ball Lightning

It has been suggested¹⁻³ that ball lightning consists⁴ of a plasma vortex ring, but an appropriate mechanism for the formation of this plasma configuration at the time of a lightning discharge has yet to be proposed. A vortex ring in a fluid may be produced by the application of an asymmetric impulse; the detonation of an explosive on a flat surface, for example, sometimes produces smoke rings. I suggest that ball lightning may be produced by a process similar to the ablation of a solid surface by a high power laser pulse.

Nilsson *et al.*⁵ have shown that stimulated emission may occur in air at atmospheric pressure. They used a discharge tube, constructed from a stack of aluminium oxide disk capacitors, with a central hole 4 mm in diameter. The stack was 102 mm long and had a total capacitance of 1 pF. With a charging voltage of 50 kV, stimulated radiation pulses of power 25 kW and duration 1 ns were obtained. The beam divergence was of the order of 10 mrad and the spectral lines showed the narrowness associated with stimulated emission. The current pulse of 10 kA was comparable in magnitude with that of a lightning discharge, but its duration of 30 ns was considerably less than for lightning. The electric field in the discharge was of the same order as in lightning although the lightning channel has a length about 10^4 times that of the superradiant discharge tube. The energy available in a thundercloud is, however, of the order of 10^9 J so that a low efficiency of conversion of electrical energy to radiation would be sufficient to produce the energy attributed to ball lightning. As a lightning channel follows a zigzag path, radiation may escape at the ground and cloud terminations or from any part of the channel where there is a change in direction.

A plasma vortex ring structure requires an appropriate magnetic field but it has been found⁶ that there are azimuthal magnetic fields of several kgauss around laser produced plasmas. Deuterium plasmas with densities greater than 10^{20} cm⁻³ have been achieved⁷ with laser energies of 50 J so it is reasonable to expect a few cm³ of highly luminous plasma to be generated by conversion of less than 10^{-6} of the total electrical energy in the thundercloud to coherent radiation and then to plasma. This would entail an efficiency of conversion of electrical energy to radiation which is considerably less than the efficiency of the superradiance experiment quoted.

A photograph produced by Viemester⁸ supports this proposal, for it shows lightning striking the ground with a small streamer displaced from the point of impact but in line with part of the discharge channel.

This mechanism of producing ball lightning could explain the passage of energy through windows or aircraft portholes. It would account for the production of ball lightning near to a solid surface and at a short distance from a lightning stroke.

As with so many experiments that might be carried out on ball lightning, it would be easy to set up a test for superradiant emission, but the probability of a lightning stroke appearing in the correct position relative to the equipment is negligible.

E. R. WOODING

Royal Holloway College,
University of London,
Englefield Green, Surrey

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Antimatter and Ball Lightning

Ashby and Whitehead¹ have published evidence of the observation of fluxes of photons lasting ≤ 1 s at an energy corresponding to positron annihilation, in connexion with the possibility that "ball lightning" may be associated with the existence in the terrestrial environment of small quantities ($\sim 10^{-11}$ g) of antimatter. Here I shall present evidence that fluxes of this type, at about the observed frequency, can be expected from extensive air showers caused by primary cosmic rays of energy $E_0 \sim 10^{16}$ eV.

It can be shown² that more than 90% of the energy in an air shower caused by a primary in this energy range appears in the form of superimposed electromagnetic showers from photons produced in π^0 decay. Further, recent Monte Carlo studies at this laboratory by R. L. Ford, using a program originally due to H. H. Nagel, show that in electromagnetic showers at 10^9 eV and 8×10^9 eV, about seventy-five positrons are produced for each 10^9 eV of primary energy. (These results are for lead, but will presumably not differ significantly for other materials.) As these positrons will in general be fast, only about 70% of them will annihilate at rest³, and I shall neglect the remainder. I therefore assume here that about 5.5% of the primary cosmic ray energy appears in the form of photons of energy 511 keV.

How would this radiation be distributed in space? Hayakawa⁴ gives the radius of the core of such a shower, from which an effective value of 2 m can be taken. Further, when the core hits the ground, it enters a medium where the radiation length (in m) is some three orders of magnitude shorter. Hence, for the first few radiation lengths in the ground, its longitudinal development will be typical of a solid whereas its lateral size will remain characteristic of the air. The annihilation of slow positrons will cause the isotropic emission of 511 keV photons. Because of the absorption in the ground, and solid angle effects, I shall consider only the first radiation length (~ 20 cm) of the ground. Thus a vertical shower has an approximately disk shaped source of radius $r = 2$ m, thickness ~ 20 cm. A spherical detector of radius δ at a height h above the ground will then collect a fraction

$$\frac{\delta^2}{4r^2} \log_e \left(1 + \frac{r^2}{h^2} \right)$$

of the emitted photons. If $\delta = 6$ cm, $r = 2$ m, and $h = 1$ m, this fraction is 3.6×10^{-4} .

I shall now consider the number N of photons emitted by the disk. On page 472 of ref. 4 Hayakawa gives the longitudinal development of a shower, and using this, the relative energy deposition can be approximated for simplicity by a function which rises linearly from zero to a maximum at a depth l and then declines linearly to zero at a total depth $3l$, where l is the depth of the "shower maximum" for an electromagnetic shower of the same initial energy E_0 . It can then be shown that the expected energy deposition at an atmospheric depth d will be

$$E' = E_0 \frac{(3l-d)}{3l^2}$$

per radiation length, over the range $l < d < 3l$. The number of 511 keV photons will then be $N = 0.055 E'/m_e$. The condition that $d < 3l$ defines a solid angle for acceptance

$$\Omega = 2\pi \left(1 - \frac{d}{3l} \right)$$

It turns out that

$$\bar{E}' = E_0 \left[\frac{1}{l} - \frac{d}{l(3l-d)} \log_e \frac{3l}{d} \right] = E_0 f$$

As $d = 28$ radiation lengths of air at sea level, and as l varies with $\log E_0$, it follows that the factor f is almost constant at $\sim 1/60$ for energies above $\sim 10^{15}$ eV (for which $l = 16$ radiation lengths).

The average flux of the four events seen by Ashby and Whitehead is 8,200 counts. This gives

$$\bar{N} = \frac{8,200}{3.6 \times 10^{-4}} = 2.27 \times 10^7,$$

$$\bar{E}' = \frac{m_e}{0.055} \times 2.27 \times 10^7 = 2.1 \times 10^{14} \text{ eV}$$

so that an initial energy E_0 of 1.25×10^{16} eV is required. Here $l = 18.5$ radiation lengths, so that $\Omega = 3.1$ sr. The equipment was active for $\sim 1.3 \times 10^7$ s, and if a "sensitive area" of $\sim 10 \text{ m}^2$ is assumed a total exposure of $1.3 \times 10^7 \times 3.1 \times 10 \times 10^4 = 4.04 \times 10^{12} \text{ cm}^2 \text{ sr s}$ is indicated. Hayakawa (ref. 4, page 569) gives the primary flux at 1.25×10^{16} eV as $0.6 \times 10^{-12} (\text{cm}^2 \text{ s sr})^{-1}$, so that about 2.5 events are to be expected—almost the number seen by Ashby and Whitehead.

These arguments are by no means precise, but they do indicate that substantial fluxes of 511 keV photons are to be expected in the cores of extensive air showers. Quite apart from any relevance to the question of ball lightning, this phenomenon might be of use in cosmic ray studies.

J. F. CRAWFORD

W. W. Hansen Laboratories of Physics,
Stanford University,
Stanford,
California 94305

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BIOLOGICAL SCIENCES

Enzymatic Cleavage of Methotrexate provides a Method for Prevention of Drug Toxicity

METHOTREXATE, a widely used and effective antineoplastic agent, is eliminated primarily by urinary excretion in man¹. In species such as the rabbit, which possess hepatic enzymes capable of metabolizing methotrexate to inactive products, the drug is rapidly degraded and virtually non-toxic². In species which do not metabolize the drug, such as mouse and man, the dose-limiting bone marrow and gastro-intestinal toxicity seems to result from persistence of low (10^{-7} to 10^{-9} M) plasma levels of methotrexate for many hours after its administration^{3,4}. To counteract this toxicity, 5-formyl tetrahydrofolate, or leucovorin, has been given 12–36 h after high doses of methotrexate, allowing an improvement in the drug's therapeutic index^{5,6}.

We have recently isolated an enzyme from a strain of *Pseudomonas stutzeri*, carboxypeptidase G₁ (CPD G₁), which hydrolyses the C-terminal glutamyl groups from peptide linkage such as found in folic acid⁷. This enzyme has antitumour activity against rodent leukaemias as the result of its ability to lower serum folate levels. Other glutamyl-terminal substrates, such as methotrexate, the N⁻¹⁰ methyl derivative of folic acid, are readily degraded by this enzyme. We report here studies in mice indicating that highly purified CPD G₁, administered at times after methotrexate, may rapidly destroy the folate antagonist and prevent its toxicity.

BDF₁ male mice, 20–25 g, were used. Agents were injected intraperitoneally in a volume of 0.01–0.02 mg/g body weight. Purified CPD G₁, specific activity 200 U/mg protein or greater, was used. Concentrations of methotrexate were determined by the dihydrofolate reductase inhibition assay after diluting plasma 1:4 with water and heating to 80° C for 10 min to destroy CPD G₁ activity⁸.

Initial experiments defined the plasma disappearance of methotrexate (Fig. 1). Following the injection of 1,000 mg/kg, methotrexate concentration in plasma remained above 10⁻⁸ M for 3 days. A single dose of CPD G₁, 800 U/kg, 24 h after methotrexate, produced an immediate decrease in the plasma level of methotrexate, although a delayed return of low levels of methotrexate to plasma was detected 12–24 h after enzyme administration (Fig. 1a). The source of this residual methotrexate was presumed to be a site inaccessible to CPD G₁, such as the lumen of the gastro-intestinal tract. CPD G₁ completely cleared methotrexate from plasma in animals treated with 350 mg/kg (Fig. 1b).

Further experiments demonstrated that CPD G₁, given 24 h after methotrexate, completely protected mice from the lethal toxicity of 350 mg/kg (an LD₅₀ dose), and increased the number of survivors from 22 to 50% in animals treated with 1,000 mg/kg (Table 1). A second dose of CPD G₁ at 48 h, which hydrolysed methotrexate returning to the plasma after the first enzyme dose, further increased the survival rate to 94%. In spite of its salutary effect on survival, CPD G₁ did not prevent weight loss in either the 350 or 1,000 mg/kg groups.

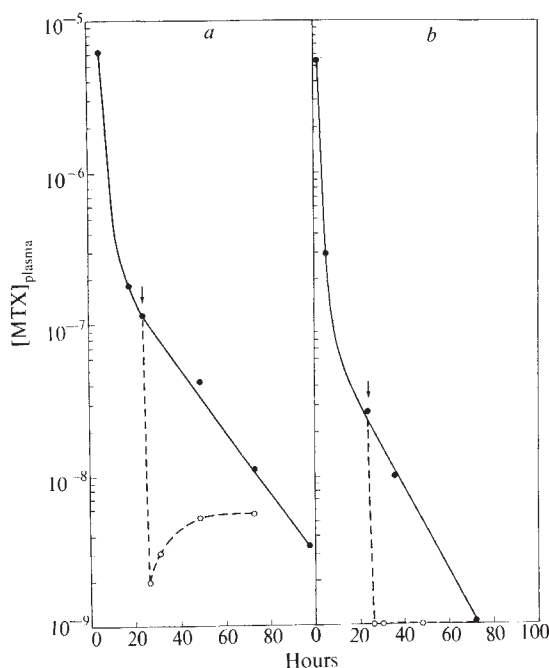


Fig. 1 Effect of CPD G₁ on plasma concentration of methotrexate (MTX). a, ●, 1,000 mg/kg methotrexate, time 0; ○, 1,000 mg/kg methotrexate, time 0; and 800 U/kg CPD G₁, 24 h (↓). b, ●, 350 mg/kg methotrexate, time 0; ○, 350 mg/kg methotrexate, time 0; and 800 U/kg CPD G₁ at 24 h (↓).

Table 1 Toxicity of Methotrexate ± CPD G₁

Dose of methotrexate, day 0 (mg/kg)	CPD G ₁ (U/kg)	Δwt, day 3 (%)	Survivors (%)
350	—	-12	5/8 (62/5)
350	800, day 1	-12	8/8 (100)
1,000	—	-14	7/32 (22)
1,000	800, day 1	-12	8/16 (50)
1,000	800, day 1+2	-12	16/17 (94)

Mice were observed for 60 days to verify survival.

To determine whether sequential therapy with methotrexate and CPD G₁ could be used to improve survival of tumour-bearing animals, mice inoculated with 10⁵ L1210 leukaemia cells were given a single dose of methotrexate on day 3. One group of animals then received no further therapy, while a second received CPD G₁ on day 4, and a third was given leucovorin on day 4. With increasing doses of methotrexate, a progressive increase in median life span was achieved until toxic dose levels were reached (Fig. 2). Mice receiving 500 or 1,000 mg/kg died 3–5 days after methotrexate injection due to drug toxicity. Mice which were given CPD G₁ on day 4 tolerated 500 and 1,000 mg/kg well, there being only one toxic death in the latter group of eight animals; in these mice there was a further increase in median life span to a maximum of 90% for those treated with 1,000 mg/kg methotrexate. There was no difference in the survival of animals treated with leucovorin or CPD G₁ on day 4, after receiving methotrexate on day 3. However, at every dose of methotrexate the combination of antifolate and CPD G₁ produced a prolongation of life span greater than that produced by methotrexate alone, suggesting a possible antitumour effect of the enzyme, although in the conditions used in these experiments there was no increase in life span in control animals treated solely with single doses of CPD G₁.

A potential disadvantage of leucovorin protection is that the reduced folate may partially reverse the established antitumour effect of the folate antagonist⁹. It was thus important to determine whether CPD G₁, by hydrolysing intracellular methotrexate bound to dihydrofolate reductase, would have a similar undesirable effect. This seemed unlikely because the enzyme, with a molecular weight of 90,000, would not be expected to penetrate the cell membrane¹⁰. To determine whether hydrolysis of bound methotrexate takes place *in vivo*, a small dose, 5 mg/kg, was given to two groups of mice. At this dose, methotrexate was completely eliminated from plasma within 15 h, but significant amounts of drug persisted in the liver bound to dihydrofolate reductase. In animals treated with CPD G₁ 24 h after methotrexate there was no change in the intrahepatic levels of drug compared with the control group, indicating that intracellular methotrexate, bound to reductase, was inaccessible to CPD G₁ (Table 2). The failure of CPD G₁ to hydrolyse hepatic methotrexate seems to result from the enzyme's inability to penetrate the cell membrane,

Table 2 CPD G₁ Hydrolysis of Methotrexate Bound to Reductase *in vivo*

	Group 1	Group 2	Group 3
Treatment:			
Methotrexate 5 mg/kg at time 0	+	+	—
CPD G ₁ 800 U/kg at 24 h	—	+	+
Hepatic methotrexate* at 48 h	97	113	0

* Expressed as μmol/mg hepatic protein.

Three mice were used in each group. Protein-bound methotrexate was released from liver by homogenizing in 5 ml. water at 0° C, diluting to 25 ml. with water, and heating to 80° C for 15 min. The supernatant was spun down at 40,000g and assayed for methotrexate. Protein was determined by Lowry's method¹¹.

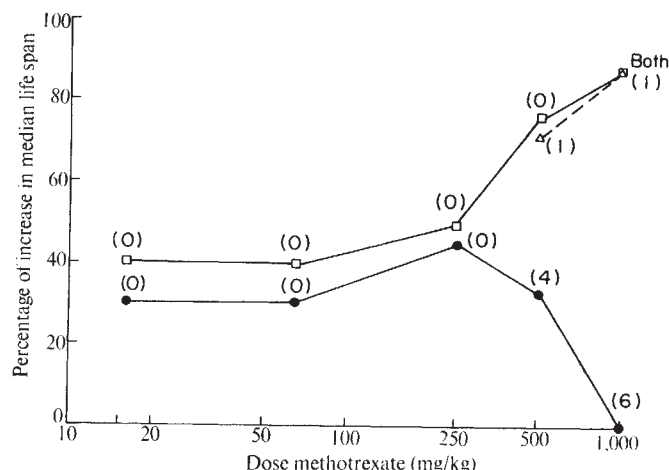


Fig. 2 Treatment of leukaemia L1210. Eight male BDF₁ mice were inoculated with 10⁵ leukaemia L1210 cells in each group. ●, Methotrexate alone; □, methotrexate plus 800 U/kg CPD G₁, day 4; △, methotrexate plus 4 mg/kg leucovorin, day 4. Figures in parentheses represent deaths due to drug toxicity.

Table 3 Hydrolysis of Methotrexate Bound to Reductase

	1	2	3
TPND (0.07 µmol)	+	+	+
Reductase (0.003 U)	+	+	+
Methotrexate (1.2 µmol)	+	+	+
CPD G ₁ (2.4 U)	+	+	—
Methotrexate remaining after 30 min incubation at 37° C (%)	5	15	100

The indicated components, plus Tris-Cl, 0.05 mmol, pH 7.5, and KCl, 0.15 mmol, were incubated in a total volume of 1 ml. at 25° C for 5 min. CPD G₁ was then added and the solution incubated at 37° C for 30 min. The enzymes were inactivated and protein-bound methotrexate was released by heating to 80° C for 15 min.

in that the enzyme was able to hydrolyse methotrexate bound to reductase in a cell free system (Table 3)

These experiments have shown no difference in the survival of animals treated with methotrexate CPD G₁ as opposed to methotrexate-leucovorin. CPD G₁ has several possible advantages in that it does not reverse the established intracellular blockade of DNA synthesis, as does leucovorin, and possesses antitumour activity of its own. Finally, the enzyme has a brief 4–6 h half-life in mice, compared with the longer 12 h half-life of leucovorin⁴, and thus would not interfere with subsequent doses of methotrexate. Leucovorin has the obvious advantages of being inexpensive and non-immunogenic. The relative merits of these two forms of methotrexate "rescue" will require further evaluation. However, the studies reported here do illustrate a new method for preventing drug toxicity and improving therapeutic results by the administration of a purified heterologous drug-metabolizing enzyme.

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B. A. CHABNER
D. G. JOHNS

Laboratory of Chemical Pharmacology,
National Cancer Institute,
National Institutes of Health,
Bethesda, Maryland 20014

J. R. BERTINO

Department of Pharmacology,
Yale University,
School of Medicine,
New Haven, Connecticut 06510

Received May 24, 1972.

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Methadone Induced Mortality as a Function of the Circadian Cycle

METHADONE maintenance is an increasingly used approach in heroin addiction^{1,2}. Because addicts are often provided with a number of days' supply of methadone for unsupervised use, problems of overdosage are becoming prevalent^{3–5}. The effectiveness of many drugs is closely related to the circadian rhythm^{6–8}, and it is important to evaluate methadone overdosage as a function of the circadian cycle.

A project designed to study variations in methadone sensitivity at specific times of day was undertaken. Seven groups of albino rats, WRC stock from the Walter Reed Army Institute of Research production colony, of similar genetic background, sex, weight, age, and past history were selected. For at least one week before each study, the rats were maintained on a regimen standardized for periodicity analysis—twelve hours of light (from 0800 to 2000 h) alternating with twelve hours of darkness (from 2000 to 0800 h). Room temperature was monitored but allowed to fluctuate normally as an additional *zeitgeber*, and Purina chow and water were freely available at all times. Methadone hydrochloride was administered by intraperitoneal injection in 1 ml. saline solution. The same handler was used for all rats. The laboratory and adjacent observation room were kept at the same temperature as the standardized colony room. The injected rats were observed for at least 45 min following administration of the drugs. Those rats which died in less than three hours following injection were included in the mortality series (all mortalities did in fact occur within the three hours).

Based on previous cited work with similar toxic agents, we estimated the maximally sensitive period of the circadian cycle to be the beginning of the rat's activity period. The first group of forty rats was selected for a pilot study to establish a dose lethal to 70% of the population (LD₇₀) at this time. The rats were injected according to a varying dosage schedule and a standard dose-response curve was obtained. From these data we calculated LD₇₀ to be 47 mg/kg.

The rest of the rats were divided into six groups. At time periods of 0100, 0500, 0900, 1300, 1700, and 2100 h, a subgroup of seven animals was removed individually from the standardized colony room and injected with 47 mg/kg of methadone hydrochloride. Mortality statistics were gathered. The data in Table 1 were collected on four different days over a period of two months.

Behavioural observations were also made in groups showing toxicity after injection. Most characteristic was an immediate withdrawal to a corner of the cage, followed by a cessation of spontaneous motion and a tonic extension of the tail. The rats then developed decreased responsiveness to visual and tactile stimuli and an initial hyperexcitability to auditory stimuli.

Table 1 Methadone Mortality Statistics for Six Groups of Rats

Time of day	n	Survivals	Mortalities	Mortalities (%)	Standard error (%)
0100	26	5	21	80.8	± 7.0
0500	26	9	17	65.4	± 8.8
0900	25	4	21	84.0	± 7.0
1300	25	6	19	76.0	± 8.3
1700	25	4	21	84.0	± 7.0
2100	26	3	23	88.5	± 5.4

Many of the rats also had clonic convulsive episodes prior to their death.

Susceptibility to methadone varies as a function of the time of administration, with the rats most sensitive at the onset of their activity period, 2100 h, and most resistant toward the latter portion of their activity period, at 0500 h (Fig. 1). A chi-square test was used to determine the statistical significance between the hours having the highest and lowest mortality. Statistical significance was evident at $P < 0.05$ with one degree of freedom. Further analyses showed this significance to be primarily attributable to the higher resistance to the drug at 0500 h. The chi-square test comparing the lowest mortality group with the remainder of the curve was significant at $P < 0.05$. A comparison with the highest mortality group was significant at only $P < 0.30$.

This work suggests that, as with other drugs, circadian cycle does influence the effectiveness and lethality of methadone. The function is cyclical in nature but not as precisely sinusoidal as might be anticipated from the literature on other agents. It is likely that by increasing the number of animals in each group, the deviations from a sinusoidal function would be significantly reduced. Alternatively, more than one effective metabolic system may be involved in establishing the animal's resistance to methadone, and these systems may not fluctuate exactly in phase with one another. The most sensitive portion of the circadian cycle appears to occur at the period of transition from rest to activity, when a number of live systems are beginning to accelerate their activities from their minimal resting levels. The most resistant period of the cycle occurs toward the end of the activity period, near the time of peak metabolic activity, when the rat is least sensitive to other toxins. This suggests that enzyme systems may be significant in susceptibility to methadone.

Extrapolation to the human system must be undertaken with caution and should include more sensitive measurements of behavioural and physiological drug effects on humans. For example, many methadone programmes dispense the drug in

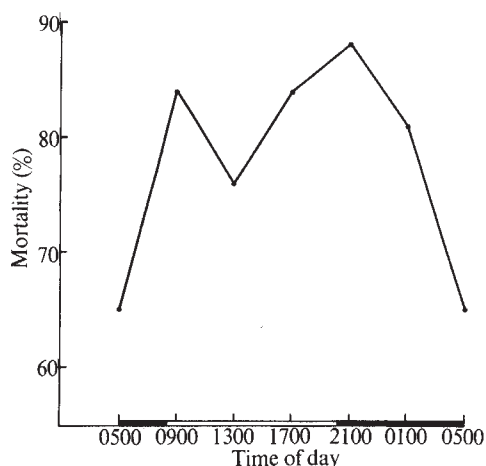


Fig. 1 % mortality of six groups of rats injected at different times of day. Photoperiod of the light-dark cycle was from 0800 to 2000.

the morning. Since the rat is a nocturnal mammal, this time corresponds to the suggested most sensitive period for humans. The attempts to titrate methadone dosage at this time, to prevent withdrawal and maintain continuous "heroin blocking effect"⁹, might imply suboptimal methadone levels later in the day. Furthermore, giving methadone in the morning may result in a maximal narcosis at the beginning of the work day. These issues could be of value in the design of more effective rehabilitative efforts.

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ROBERT H. LENOX

Department of Psychiatry and Neurology,
Walter Reed General Hospital,
Washington DC 20012

THOMAS W. FRAZIER

Behavioral Technology Consultants

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Segregation and Sedimentation of Red Blood Cells in Ultrasonic Standing Waves

THE formation of bands of red cells in the blood vessels of live chick embryos during ultrasonication has been reported by Dyson, Woodward and Pond¹. It was suggested that the segregation was primarily caused by Bernoulli forces between the cells owing to the displacement of the cells relative to the plasma, and that the standing wave was operative only in fixing the position of the segregation pattern. Here we suggest that it is primarily the standing wave which is the cause of the segregation.

During sonication of whole blood and whole blood cultures in polystyrene containers at intensities of about 3 W cm⁻² at 1 MHz, the natural sedimentation of the red cells is greatly accelerated. On resuspension of the red cells, the sedimentation time in the absence of sonication returns to normal. Viscosity measurements made on the blood and the plasma during sonication show no significant change. In sonicated blood cultures, where the density of red cells is relatively low, the red cells segregate into bands at right angles to the direction of propagation of the ultrasound and with a half wavelength periodicity clearly related to the existence of acoustic standing waves. This effect also exists in whole blood during sonication, but is evident only when very small containers (1 mm thick) are used, as the higher density of red cells tends to mask the effect. Increased sedimentation is observed when the segregation bands are in a vertical plane. On re-orientating the sonication so that the bands are horizontal there is no apparent increase in sedimentation. This suggests that the increase in sedimentation rate is due to convection currents caused by the periodic variation of density of the cell suspensions (Fig. 1).

Microphone and sensitized thermistor probe scans within the containers show the presence of standing waves. If the hard polystyrene containers are replaced with cells made from

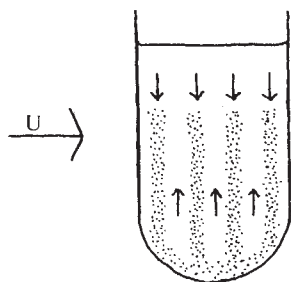


Fig. 1 Schematic diagram of segregation and sedimentation of red blood cells. Arrows denote convection currents. U, Direction of ultrasound.

polythene membrane about 10μ thick, no standing wave, no increase in sedimentation rate and no segregation can be detected for intensities up to 5 W cm^{-2} . When an acoustic reflector, however, is placed behind the cell (Fig. 2) to create a standing wave, almost instantaneous segregation and rapid sedimentation occur. Moving the polythene cell along the axis of propagation causes the segregation to move relative to the cell, but remain stationary relative to the reflector and transducer. It is necessary to establish a "dose response" of red cell segregation to the magnitude of the standing wave and relate this to standing waves which might exist in the body during clinical use of ultrasound. The segregation times determined for a range of transducer voltages for both whole blood and the 1:10 blood/plasma are shown in Fig. 3. The abscissa show the intensity of a plane progressive wave which, if totally reflected, would result in the segregation time shown on the ordinate. Segregation was detected by viewing the transmission of an intense focus light beam through the cell at right angles to the ultrasound propagation direction. This criterion is arbitrary but leads to reproducible results for segregation times. The experimental intensities were measured by a swinging ball radiation balance² and extrapolated for intensities too low for the balance to measure. The intensities may be compared directly with those quoted for clinical use, since clinical machines are calibrated in terms of progressive wave intensity. With the exception of tissue/air interfaces, however, there is not 100% reflexion from other boundaries within the body. The progressive wave intensity must be increased by a factor of $1/R$, where R is the intensity reflexion coefficient, to produce a standing wave of the same amplitude.

Segregation occurs in whole blood within 30 s at intensities as low as 20 mW cm^{-2} . In 1:10 blood/plasma segregation will occur at 3 mW cm^{-2} and this figure might apply to whole blood were it not for the masking effect of the high density of red cells. These intensities are below those used clinically for foetal pulse detection and far below therapeutic intensities.

These observations raise two questions. First, what standing

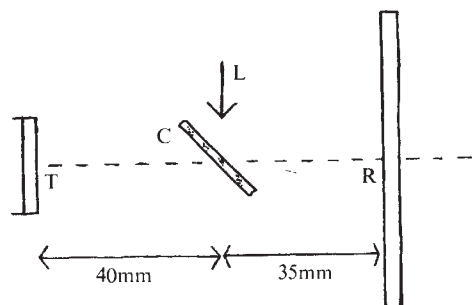


Fig. 2 Arrangement for measuring segregation time as a function of progressive wave intensity. Reflector is removed for intensity measurement. T, Transducer; C, polythene film cell; L, illuminating light beam; R, acoustic reflector.

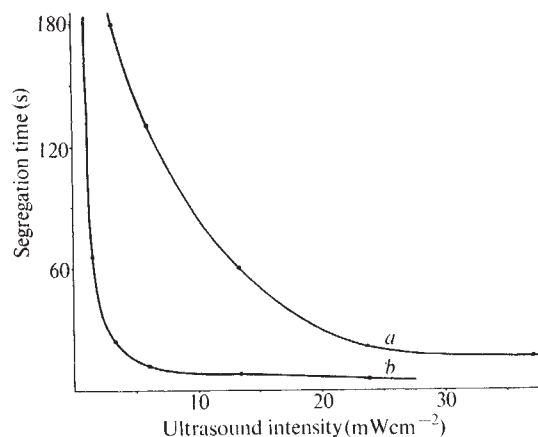


Fig. 3 Time for visible segregation as a function of plane progressive wave intensity, for 100% reflexion. a, Whole blood; b, 1:10 blood/plasma.

wave amplitudes are likely to occur in the body during clinical use of ultrasound? Second, to what extent does the segregation constitute a hazard and to what extent is it nullified by normal blood flow? Before these questions can be answered, a back absorber must be used on the opposite side of the patient from that to which the transducer is applied, to eliminate the almost 100% reflexion at the body/air interface.

Work by Dyson *et al.* suggests that the red cell segregation is broken down very rapidly by normal heart action, even at high intensities. The extent to which this is so in fine capillaries must be investigated, as a barrier of high viscosity such as the segregation band would present a much higher impedance to flow. That the segregation time is reduced when the density of red cells is reduced is not consistent with the suggestion that segregation is due to Bernoulli forces. These mutually attractive forces would be diminished by increasing the average distance between the red cells and would lead to an increase in segregation time.

N. VASHON BAKER

Department of Plant Biology and Microbiology,
Queen Mary College, University of London,
Mile End Road,
London E1 4NS

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Stimulation of the Sodium Pump in the Red Blood Cell by Lithium and Potassium

THE efflux of the ^{22}Na at 37°C from normal human red blood cells incubated with ^{22}Na into media containing different concentrations of potassium and lithium has been studied. Lithium at concentrations of 3 mM and 6 mM causes a significant stimulation of efflux, when the concentration of potassium is zero or 2 mM, but the effect of lithium is not apparent in the presence of 6 mM potassium which itself causes a big stimulation. This stimulation of the sodium pump by extracellular lithium may explain observations of a low intracellular sodium concentration under such conditions. It may be relevant to the prophylactic action of lithium salts in manic-depressive disease.

A deficit in sodium transport has been reported in some patients with depressive illness¹⁻³, and the administration of

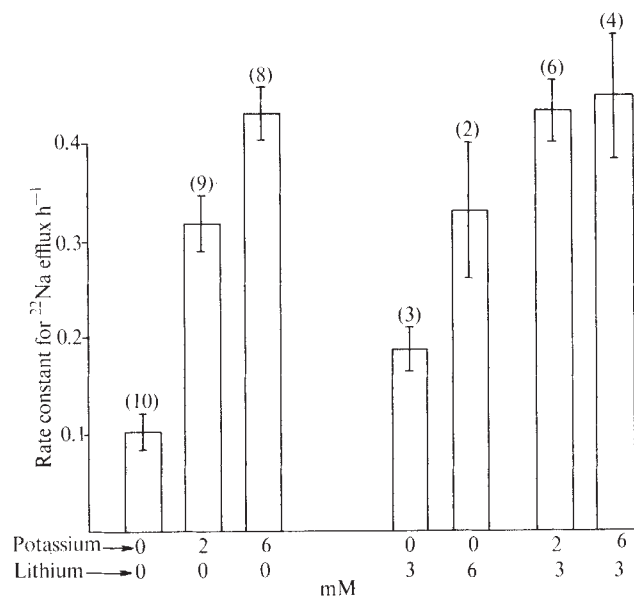


Fig. 1 Rate constants for ^{22}Na efflux from normal human red cells incubated in media containing various concentrations of potassium and lithium. The figures in parentheses above each column indicate the number of experiments in each group. The concentrations of potassium and lithium in the media are shown below each column.

lithium has been observed to reduce intracellular sodium as measured by the ^{24}Na and ^{82}Br spaces^{4,5}. A similar reduction in the intracellular sodium concentration in rabbits infused with lithium chloride has been noted by direct analysis of skeletal muscle⁶ and there is a reduction in total brain sodium in rats receiving a lithium diet⁷. A possible mechanism for this might be a stimulating effect of lithium on the sodium pump.

The red blood cell is peculiarly suitable for studying the sodium pump and, in lactose treated red cells which have been loaded with sodium, lithium can to some extent be substituted for potassium as an external cation promoting sodium efflux^{8,9}. Its effect under these conditions is small.

The experimental model presented here has been designed to simulate more the situation existing during administration of lithium to man. Human red blood cells have been loaded with ^{22}Na and the efflux of this radioisotope into a sodium chloride medium containing low concentrations of lithium and/or potassium studied. Potassium is present externally *in vivo* and the pump is very sensitive to its external concentration over the range 3–5 mM (ref. 9).

The technique used was basically that of Sachs and Welt¹⁰ modified by Smith and Samuel¹¹. Heparinized blood (10–12 ml.) was obtained from normal subjects and immediately centrifuged. The cells were incubated at 37° C for 3 h with 25 μCi ^{22}Na in a phosphate buffer. After this loading period, the extracellular ^{22}Na was washed off with six washes in isotonic magnesium chloride. The loaded red cells were then incubated in the test media and the efflux measured in samples by subtracting the radioactivity in supernatant from the total radioactivity of the sample. Care was taken to keep the haematocrits of the red cells in the incubation media at or below 0.2% to minimize the effect of potassium efflux from the red cell sample. The test media used contained KCl and/or LiCl and an appropriate NaCl concentration, in addition to phosphate buffer and dextrose. Seven media of different lithium and potassium concentrations were used, as shown in Table 1.

Rate constants can be obtained from the slopes of the lines relating I_n (activity remaining in cells) to time. There was a slight tendency for the slopes of these lines to decrease with time between 0 and 60 min; the difference between the logarithms of the activities in the cells at 0 and 60 min was used to calculate the rate constants given in Fig. 1.

Table 1 Test Media, showing Li and K Concentrations

	K mM	Li mM
A K free, Li free	0	0
B Low K	2	0
C High K	6	0
D K free, low Li	0	3
E K free, high Li	0	6
F Low K with Li	2	3
G High K with Li	6	3

The histogram of the figure indicates the effect of the different media on the rate constant for efflux of ^{22}Na . Table 2 gives the probabilities for the differences between members of all possible pairs of mean rate constants being due to chance. The stimulating effect of potassium on sodium efflux is well known⁹. In the K-free medium, 3 mM Li causes a significant stimulation and 6 mM Li produces an effect as great as 2 mM K. In the presence of 2 mM K, 3 mM Li again causes a significant additional increase. At 6 mM, the effect of potassium itself is so great that no further stimulation by lithium is seen.

The effect of potassium on sodium efflux is thought to be largely on the active energy dependent component, the transport ATPase, being activated by external potassium¹². It is likely that the effect of lithium has a similar basis. If extracellular lithium does stimulate sodium pumping, this may be the cause of the low intracellular sodium concentrations observed in animal tissues in the presence of more than 3 mM of lithium in the extracellular fluid⁶. It is important to find whether this effect is still present at lithium levels in the range 0.8–1.2 mM, that is, at concentrations which can be tolerated in man and have been shown to be effective in the treatment of manic-depressive illness.

Table 2 P Values for Differences between Mean Rate Constants in Different Media

Medium	A	B	C	D	E	F	G
A	—	<0.001	<0.001	<0.05	<0.01	<0.001	<0.001
B		—	<0.05	<0.1	NS*	<0.05	<0.1
C			—	<0.01	NS	NS	NS
D				—	NS	<0.01	<0.05
E					—	NS	NS
F						—	NS
G							—

* NS: not significant.

Low intracellular sodium concentration may effect nervous activity in several possible ways. Within the axoplasm of a nerve fibre it may cause an increase in the positive overshoot of the action potential, which could modify chemical transmitter release at presynaptic endings. Accumulation of several transmitters in synaptosomes depends on the trans-membrane sodium gradient, so that uptake of the transmitter in presynaptic endings as well as its release may be affected¹³. There is evidence that amine levels and turnover in the hypothalamus and brain-stem may be altered by lithium administration¹⁴. More directly, the threshold of certain responses to sensory stimulation is reduced by lithium dosage in rats and the situation may be reversed by giving 5-hydroxytryptophan¹⁵. Such effects of lithium on amine metabolism could well be mediated through a depression of the intracellular concentration of sodium.

A. I. M. GLEN*
M. W. B. BRADBURY
JANET WILSON

Sherrington School of Physiology,
St Thomas's Hospital Medical School,
London SE1

Received July 10, 1972.

* Present address: MRC Brain Metabolism Unit, Department of Pharmacology, University of Edinburgh, 1 George Square, Edinburgh EH8 9JZ.

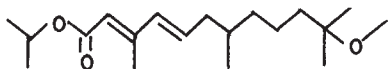
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Evidence of Cross-resistance to a Juvenile Hormone Analogue in Some Insecticide-resistant Houseflies

THE widespread occurrence of resistance to present-day insecticides among pest species^{1,2} has prompted intensive research into alternative means of insect control. The discovery that application of the insect juvenile hormone (JH) or its mimics at certain critical stages of the life cycle leads to developmental abnormalities and death³ has raised hopes of the emergence of a "third generation" of pesticide chemicals⁴. It has been suggested that insects would be unable to develop resistance to their own juvenile hormone³. Arguments have also been advanced that resistance to hormonal insecticides is not unlikely^{5,6}.

We have been studying the possibility that insects may develop resistance to juvenile hormone analogues (JHA), and here we report the presence of varying levels of cross-resistance to one such compound in certain insecticide-resistant strains of the housefly.

The juvenile hormone analogue ZR-0515 (isopropyl 11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate) was supplied by the Zoecon Corporation, Palo Alto, California. It shows outstanding activity against houseflies, even at concentrations below those required of such potent insecticides as dimethoate (LD_{50} 0.011 μ g/adult ♀) and naled (LD_{50} 0.026 μ g/adult ♀) which are now employed in fly control.



Flies were reared on standard CSMA media at 27° C and 70% RH. The JHA was applied in acetone solution on 0.5 μ l. volumes to <2-h old unsclerotized pupae, that is, during the period of highest sensitivity to the compound⁷. Treated pupae were kept in screened paper cups under a 12:12 h photoperiod at 27° C. Humidity fluctuated from 60% during photophase to 95% during scotophase. Controls, treated with 0.5 μ l. acetone, were maintained in every test and were utilized in correcting the experimental results. Each replication consisted of approximately 10 insects, depending on the availability of pupae, and was repeated on different days. Flies unable to escape the puparium were scored as dead. Dosage-mortality regression lines, ED_{50} (effective dose—50%), ED_{95} , and limits of significance were obtained by computer.

After preliminary tests a dose of 0.025 μ g/pupa was chosen for determining the rank of susceptibility of the available strains to the JHA. Table 1 shows the mean percentages of mortality of one susceptible (NAIDM-S) and seven insecticide-resistant strains, namely, an organochlorine-resistant (DDT/lindane-R), a carbamate-resistant (OMS-15-R) and five organophosphorus-resistant (parathion-R, Chlorthion-R, fenthion-R,

Table 1 Response of Various Strains of the Housefly to ZR-0515 at 0.025 μ g/Pupa

Strain	Number tested	Percentage mortality*
Susceptible NAIDM	60	100
Resistant		
DDT/lindane	18	100 ^a
Parathion	66	78.0 $\pm$ 8.5 ^b
Chlorthion	30	70.7 $\pm$ 13.5 ^b
Fenthion	77	63.9 $\pm$ 6.9 ^b
OMS-12 †	30	30.0 $\pm$ 5.8 ^c
OMS-15 ‡	60	18.9 $\pm$ 6.7 ^c
Dimethoate	100	14.1 $\pm$ 5.0 ^c

* Mean mortality $\pm$ standard deviation. Any two means having the same superscript letter are not significantly different at the 5% level as determined by Duncan's multiple range test.

† *o*-Ethyl *o*-(2,4-dichlorophenyl) phosphoramidothioate.

‡ *m*-Isopropylphenyl methylcarbamate.

OMS-12-R, and dimethoate-R). The dose was approximately 2.7 times the minimum required to produce complete suppression of adult emergence in the susceptible strain.

Susceptibility to the treatment varied considerably among the strains examined. Those selected for resistance to dimethoate, OMS-15 (*m*-isopropylphenyl methylcarbamate) or OMS-12 [*o*-ethyl *o*-(2,4-dichlorophenyl) phosphoramidothioate] showed the highest cross-resistance to JHA. Strains selected for resistance to fenthion, 'Chlorthion' [*o*-(3-chloro-4-nitrophenyl)-*o*,*o*-dimethyl phosphorothioate] or parathion, showed moderate cross-resistance, while the DDT/lindane-selected strain exhibited less than a 2.7 $\times$ level of cross-resistance.

It must be noted that the above strains have been under intensive selection pressure in the laboratory for over ten years, and each has attained maximal resistance to the selecting compound. The levels of resistance in the respective strains are: DDT/lindane-R, >1,000 $\times$; parathion-R, 1,643 $\times$; Chlorthion-R, >430 $\times$; fenthion-R, 435 $\times$; OMS-12-R, 88 $\times$; OMS-15-R, >100 $\times$; and dimethoate-R, 60 $\times$. Each strain also demonstrates various levels of cross-resistance to other insecticides, but in most cases resistance is highest toward the selecting compound. It may be assumed that the levels of cross-resistance to the JHA reported here represent the highest attainable as a result of the specific selection by the respective insecticide.

In subsequent tests we examined in greater detail the susceptibility of four strains to the JHA. These were the NAIDM-S, fenthion-R, dimethoate-R and SK. The latter had been colonized recently from the field and exhibited insecticide resistance at the LD_{95} level as follows: diazinon, 580 $\times$;

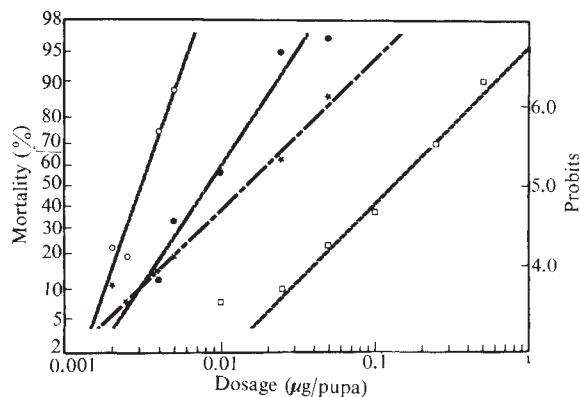


Fig. 1 Dosage/mortality relationships for pupae of susceptible (NAIDM), field resistant (SK), and laboratory-selected strains of the housefly treated with ZR-0515. ○, NAIDM-S; ●, SK (field); *, fenthion-R; □, dimethoate-R.

ronnel, 737×; fenthion, 43×; naled, 26×; and dimethoate, 15×⁸. The data in Table 2 and Fig. 1 indicate that the susceptible strain manifested a narrow range of response to the JHA, the slope of the dose-mortality regression line ($b=5.8$) being similar to that commonly obtained with insecticides. An increase in heterogeneity of response ($b=2.8$) and a relatively low level of cross-resistance to the JHA (5.05× the normal ED₅₀) are evident in the field strain. Greater heterogeneity ($b=1.9$) was found in the two laboratory-stressed strains, with accompanying resistance levels to the JHA of 39.8× (fenthion-R strain) and 150× (dimethoate-R strain).

The discovery of high levels of cross-resistance to the JHA was not entirely unexpected. In a natural system it is essential that if metamorphosis is to occur, the native JH be disposed of at the approach of and during the pupal stage. One would therefore expect that a suitable mechanism for metabolism and elimination of JH exists, and that the mechanism should attain its highest efficiency during this period. Protein synthesis in *Calpodex ethlius* was reported to reach maximum levels in the pupal stage⁹. In houseflies the levels of microsomal oxidase¹⁰, phenolase¹¹ and catecholase¹¹ were found to be highest during late larval and prepupal stages. Degradation of *Cercopia* JH injected into insects is known to occur rapidly¹², the average half life of exogenous *dl*-*Cercopia* JH applied to members of different orders of insects being 8–10 h depending on the species tested and the mode of treatment¹³.

It is perhaps unfortunate that highest sensitivity to JH in the organism coincides with the presence of greater capacity for metabolism and elimination of xenobiotics. Pupae of many species are known to require remarkably higher doses of insecticides for mortality than either the larval or adult stages^{11,14,15}. Thus the suggestion¹⁶ that research should emphasize the discovery of JH inhibitors rather than JH mimics may have considerable merit. One such inhibitor of JH in houseflies, citric acid, has recently been reported⁷.

Until biochemical evidence on the nature of the mechanisms of resistance to JHA in these strains has been obtained, any discussion must be speculative. Certain tentative suggestions, however, are evident. The presence of varying degrees of cross-resistance to JHA, irrespective of the level of insecticide resistance in each strain, suggests that several mechanisms may be involved in cross-resistance. The structure of the JHA indicates that the compound may be subject to enzymatic attack involving esterase cleavage of the ester bond, epoxidation

of double bonds followed by diol formation and cleavage, free radical formation, or demethylation, and possibly other processes. The two strains with the highest cross-resistance (dimethoate-R and OMS-15-R) probably possess an efficient amidase enzyme attacking the C-N bond of the selecting insecticides, and, conceivably, the ester bond of the JHA. Phosphatase activity, common in the organophosphorus resistant strains, probably does not play a very important role in cross-resistance to the JHA in view of the large variability of cross-resistance among the strains. Carbamate resistance is due partly to enhancement of mixed function oxidase activity and it may be assumed that the high level of JHA cross-resistance in strain OMS-15-R may also be due in part to such enzymes. Limited tests on flies reared in larval medium containing 500 p.p.m. piperonyl butoxide, an inhibitor of mixed function oxidase enzymes, however, produced only slight increase in sensitivity to the JHA. This small enhancement, however, may be due to the fact that piperonyl butoxide itself is known to induce JH symptoms in insects^{17,18}.

It is noteworthy that while high cross-resistance was observed in strains subjected to long-term specific insecticide pressure in the laboratory, the field strain examined has demonstrated only minimal cross-resistance to the JHA, despite the fact that the strain possesses the highest resistance to organophosphorus insecticides we have observed in California field populations⁸. The propensity of this strain to develop resistance by direct selection by JHA is currently being explored.

This study was supported in part by a research grant from the Environmental Protection Agency. We thank Professor R. B. March for permission to use some of the resistant strains, and Professors T. R. Fukuto and L. K. Gaston for discussion of our results. We also thank the Zoecon Corporation, Palo Alto, California, for supplying the sample of juvenile hormone mimic.

DAVID C. CERF
GEORGE P. GEORGHIOU

Department of Entomology,
University of California,
Riverside, California 92502

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Table 2 Response of Four Strains of the Housefly to ZR-0515

Dose (μg/pupa)	NAIDM- S	Percentage mortality SK- field	Fenthion- R	Dimethoate- R
0.005	0 (40)*			
0.001	4.7 (60)			
0.002	22.4 (30)	0 (50)	11.1 (50)	
0.0025	19.0 (90)	0.7 (58)	7.4 (30)	
0.004	75.1 (30)	12.1 (68)	14.6 (69)	
0.005	88.4 (90)	33.4 (111)	19.8 (104)	
0.01	99.0 (90)	57.0 (121)	37.8 (132)	7.5 (80)
0.025	100.0 (60)	95.0 (68)	63.9 (77)	10.0 (80)
0.05		96.5 (60)	87.0 (68)	22.5 (80)
0.1				37.5 (80)
0.25				69.2 (80)
0.5				90.0 (80)
Acetone control	5.5 (90)	7.9 (88)	10.1 (108)	1.3 (79)
ED ₅₀ †	0.0033	0.0084	0.0184	0.1312
ED ₉₅ †	0.0063	0.0318	0.111	0.945
Slope (b)	5.8	2.8	1.9	1.9
RR (at ED ₅₀) ‡		2.55	4.48	17.62
RR (at ED ₉₅) ‡		5.05	39.76	150.0

* Number of pupae tested.

† Effective dose for 50% or 95% mortality in μg/pupa. All ED values significantly different at 5% probability level.

‡ Resistance ratio = $\frac{\text{ED of R strain}}{\text{ED of S strain}}$

Control of *de novo* Isocitrate Lyase Synthesis in *Chlorella*

Two important hypotheses concerning the mechanism by which temporal restriction is imposed on the synthesis of enzymes during the cell cycle both suppose that enzyme syn-

thesis occurs during a period of concurrent gene transcription. Halvorson's group have made the remarkable observation that the sequence of enzyme synthesis depends on the sequence of genes on the chromosome¹, suggesting that enzyme synthesis depends on a wave of transcription passing along each chromosome. According to the other hypothesis—developed originally for prokaryotic cells^{2,3}—transcription is subject to oscillations in repression (for reviews see Mitchison⁴ and Halvorson *et al.*⁵). A quite different interpretation has also been put forward, that enzyme synthesis is determined by controls acting at the post-transcriptional level^{6,7}.

We have used the green alga *Chlorella fusca* 8p⁸ (*Chlorella pyrenoidosa* 211 8p)⁹ to test whether the temporal restriction of isocitrate lyase synthesis during the cell cycle is due to a requirement for concurrent mRNA synthesis. The enzyme is suitable, since its adaptive synthesis¹⁰ is subject to a strict temporal control with a sharp maximum rate of synthesis at 5–7 h in the 24 h cycle of growth and division¹¹. There does not seem to be the complication of control at the level of activation from precursor proteins^{12,13}, since acrylamide gel electrophoresis reveals no inactive precursor proteins in cells at those cycle stages in which no increase of isocitrate lyase activity can be obtained, although the new enzyme itself is clearly detected in cells showing an increase in enzyme activity¹¹. To further test that isocitrate lyase activity arises by activation rather than protein synthesis, we have studied the effect of metabolic inhibitors on the increase of isocitrate lyase activity in the cells at 6 h of the cycle, when they are maximally adaptive for this enzyme (see Fig. 1).

Synthesis of active enzyme is rapidly inhibited by cycloheximide, which is a specific inhibitor of protein synthesis in this organism¹⁴, and similarly by acetic acid, which is an analogue of proline¹⁵. Also, *p*-fluorophenylalanine at 1 mM (not illustrated) inhibits synthesis. These rapid inhibitions are not consistent with the presence of enzyme precursor proteins awaiting activation but support the conclusion that increasing enzyme activity requires *de novo* protein synthesis. We wondered, therefore, whether the acquisition of isocitrate lyase inducibility during the cell cycle depends on the initiation of a continuous supply of unstable messenger RNA, or on the release of translation of an existing messenger RNA.

Actinomycin, the classic inhibitor of RNA synthesis, does not affect the growth of our algae⁹, and other inhibitors are also ineffective. We have shown, however, that 6-methyl purine, which acts as an inhibitor of RNA synthesis in barley aleurone¹⁶ and in sugar cane¹⁷, immediately inhibits RNA synthesis by preventing competitively the incorporation of

adenine¹⁸. When cells synthesizing isocitrate lyase are prevented from further RNA synthesis by 6-methyl purine, enzyme synthesis continues for some time, in contrast to the effect produced by inhibition of protein synthesis (Fig. 1).

The decay of enzyme synthesis following inhibition of RNA synthesis has been taken as a measure of the persistence of mRNA in functional form, in bacterial^{19–23} and plant^{16,17} cells. For the *lac*²⁴ and *try*²⁵ operons of *Escherichia coli*, these estimates have been correlated with the level of specific hybridizable mRNA. This form of estimate is inaccurate if the enzyme undergoes an unrecognized turnover but, in this case, isocitrate lyase is stable during growth on acetate²⁶. Detailed investigation of the progress of isocitrate lyase synthesis, following inhibition of RNA synthesis, shows that the rate declines progressively (Fig. 2). The decay of enzyme synthesis allows the fitting of an exponential curve (Fig. 3a) which indicates a half-life of 36 min for mRNA in functional form. A similar estimate is obtained by considering the final observed enzyme level to be similar to the yield at infinite time, and enzyme synthesis is plotted relative to this value, in the semi-log form seen in Fig. 3b. The data yield a linear regression indicating a half-life of 34 min. The same experiment was performed with cells not synchronized with respect to division. The data shown in Fig. 4 indicate the similar half-life of 26 min for the survival of the mRNA. We conclude therefore that instability of this mRNA is a general feature of all stages of the cell cycle.

There is no evidence that the decline in isocitrate lyase synthesis is simply a direct inhibition of total protein synthesis by 6-methylpurine, since the incorporation of ¹⁴C-phenylalanine into protein in cells at the same stage of the cell cycle declines much more slowly, with a half-life of 66 min¹⁸, presumably indicating the presence of mRNA species more stable than the one for isocitrate lyase.

Synthesis of isocitrate lyase in *Chlorella* therefore appears to depend on a continued synthesis of an unstable mRNA, supporting those hypotheses of temporal control that suppose transcription during the period of enzyme synthesis. These data therefore do not support the suggestion of Sussman⁷ that the control of enzyme synthesis during the cell cycle occurs during translation. This hypothesis was drawn originally from an analogy with the morphogenesis of *Dictyostelium*, in which

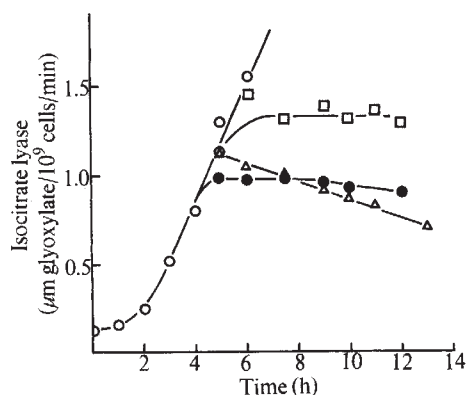


Fig. 1 Development of isocitrate lyase activity in cells at 6 h of the standard growth cycle¹¹, when aerated in the dark with 5 mM sodium acetate (○). At 4 h, subcultures received the following metabolic inhibitors: (□) 1 mM 6-methylpurine, (●) 3 μg/ml. cycloheximide, and (△) 1 mM acetic acid. Samples removed for enzyme assay were frozen in capped vials in frozen CO₂-alcohol mixture and assayed for isocitrate lyase activity by the frozen cell method as described previously¹¹. None of the metabolic inhibitors affected the catalytic activity of isocitrate lyase.

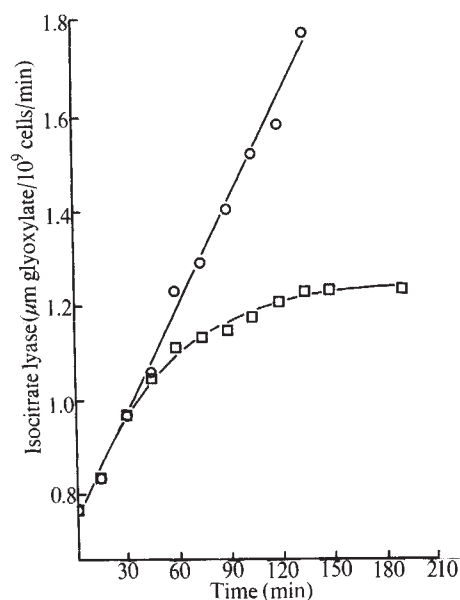


Fig. 2 Synthesis of isocitrate lyase in cells previously transferred, at 6 h in the cycle to 4 h aeration in the dark with acetate, as in Fig. 1. Incubation was continued during the sampling period with no further addition (○), or with 1 mM 6-methylpurine (□). Samples were removed for isocitrate lyase assay as in Fig. 1.

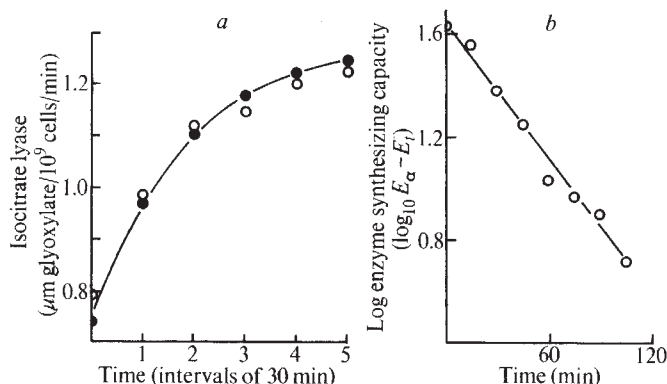


Fig. 3 *a*, Asymptotic regression curve of the form $y = A - B(e^{-t})$ fitted to the data in Fig. 2 by a method of least squares²⁶, where y = enzyme activity at time t and A is the activity approached at infinite time. For ease of computation, time was measured in units of 30 min. $\circ$, Observed values; $\bullet$, expected values, calculated from the fitted regression curve $y = 1.285 - 0.543(0.582^t)$. *b*, Semi-log plot of the data in Fig. 2. The linear regression has $P = 0.001$, assuming equality of variance.

inhibition of RNA synthesis suggests that stable mRNAs accumulate several hours before translation. The analogy cannot be discounted, however, because Tomkins's group have reported that inhibitors of RNA synthesis and hormones can increase the yield of tyrosine transaminase activity in synchronously growing rat hepatoma cells, presumably by acting on a repressor of translation⁶.

Although our observations appear to suggest that *Chlorella*, which is very different from yeast, depends on transcription as the mechanism determining enzyme synthesis during the cell cycle, we cannot rule out the possibility that this is also determined by gene sequence.

Isocitrate lyase synthesis is subject to catabolite repression²⁸. Cells which are provided with acetate do not make isocitrate lyase if they are also provided with glucose or allowed to

photosynthesize¹², and, remarkably, isocitrate lyase synthesis immediately ceases when glucose is supplied to cells that are making isocitrate lyase at the maximum rate (Fig. 4). This rapid inhibition by glucose of further enzyme synthesis contrasts with the gradual inhibition produced (in the same experiment) by inhibition of transcription and reveals that isocitrate lyase mRNA is not translated into active enzyme under conditions of glucose repression. Conditions permitting photosynthesis also immediately arrest mRNA expression.

Our observation that catabolite repression can be imposed on existing mRNA contrasts with the mechanism which operates on the *lac* operon of *E. coli*, where a decline in cyclic AMP levels^{31,32} stops transcription; repression develops as the level of *lac* mRNA declines³³. Cyclic AMP can reverse the catabolite repression of bacterial enzymes³⁴, but neither cyclic AMP, nor the more permeable dibutyl form, could relieve the glucose repression of isocitrate lyase synthesis in *Chlorella*. There have, however, been previous reports that post-transcription controls can contribute to catabolite repression. In *E. coli* cyclic AMP can increase the yield of β -galactosidase³⁵ and tryptophanase³⁶ even after transcription has been blocked. The only observation directly comparable to the phenomenon described here is that the synthesis of α -glucosidase in yeast can be blocked by high concentrations of glucose although mRNA is present³⁷.

We conclude that the adaptive synthesis of isocitrate lyase during the cell cycle is *de novo* and depends on periods of concurrent gene transcription. Although post-transcriptional control is detected, it operates as an override to prevent gene expression when the enzyme is redundant. It will be interesting to determine whether the programmed transcription of mRNA remaining latent under post-transcriptional control is employed for other enzymes.

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W. McCULLOUGH
P. C. L. JOHN

Department of Botany,
Queen's University,
Belfast BT7 1NN

Received July 10, 1972.

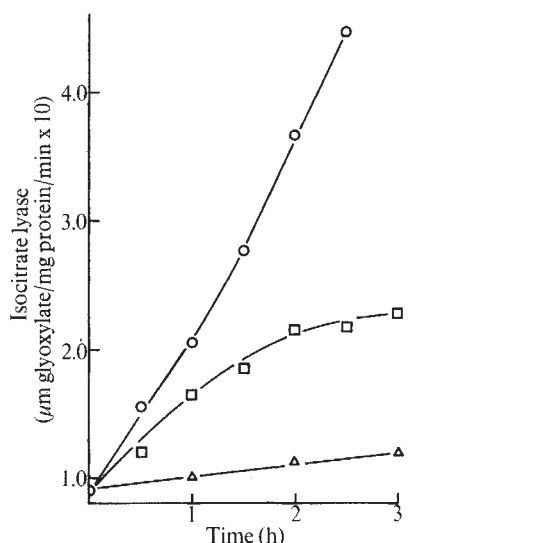


Fig. 4 Synthesis of isocitrate lyase in cells previously transferred, at 6 h in the cycle, to 4 h aeration in the dark with acetate, as in Fig. 1. Incubation was continued during the sampling period with: no further addition ($\circ$); 1 mM 6-methylpurine ($\square$); or with 30 mM glucose ($\triangle$). Cells sampled for enzyme assay were washed in cold 0.025 M imidazole HCl, pH 6.8, 5 mM MgCl_2 and then broken in the same buffer containing 2 mM dithiothreitol, by passage twice through a French pressure cell at 0°C . Debris was pelleted by centrifugation at $100,000g$ for 5 min at 4°C and isocitrate lyase was assayed in the soluble fraction by the method of Kornberg²⁹, as described previously¹¹. Protein was assayed with Folin Ciocalteu reagent³⁰.

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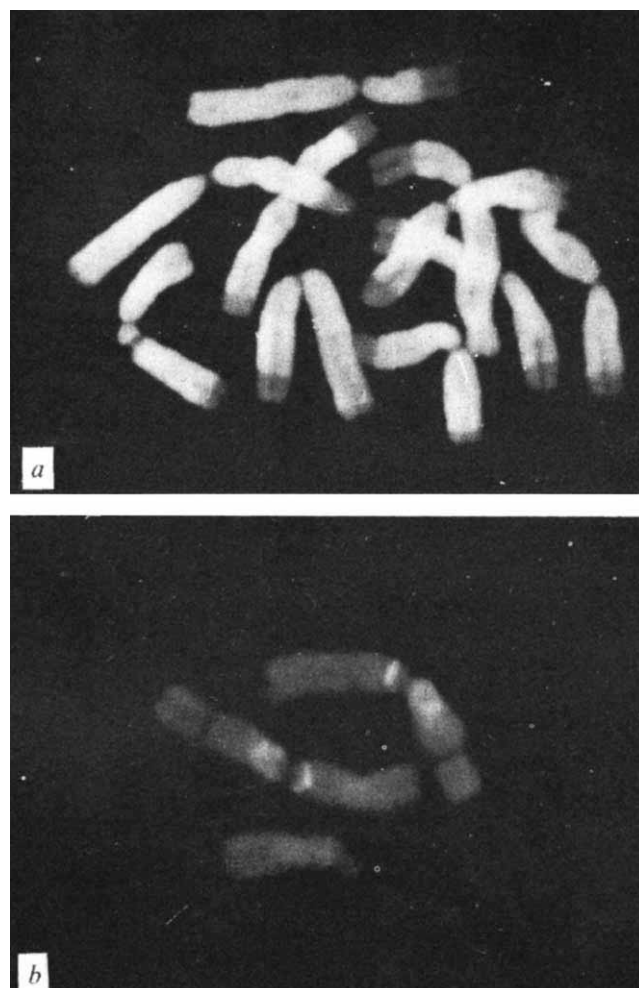


Fig. 1 *a*, Mitotic metaphase chromosomes of *Tulbaghia alliacea* stained with the alcoholic extract of *Chelidonium majus*. Note the distally located regions of reduced fluorescence. *b*, Two M and one S chromosomes of *Vicia faba* stained with an alcoholic extract of *Macleaya cordata*. The intense fluorescence pattern is the same as that obtained with quinacrine staining.

quinacrine but was orange-red to golden-yellow instead of yellow-green. It showed exactly the same banding patterns as in preparations stained with quinacrine (Fig. 1*a* and *b*) and could be used for the detection of Y-bodies.

The extracts from the two species of *Papaver* gave yellowish-orange fluorescence of medium intensity showing the quinacrine bands but giving uncertain results in the detection of the Y-body in buccal smears. All the extracts from the other plants species, including those belonging to the Fumariaceae, gave

Quinacrine-like Fluorescence of Extracts from Papaveraceae and Fumariaceae

THE introduction of certain DNA-binding fluorochromes for the analysis of chromosome structure in plants and animals^{1,2} has led to experiments aiming to discover other fluorescent compounds having such specificity. A preliminary investigation of the properties of the fluorescence of extracts from various plant species has been initiated at the Botany School, Oxford, and at the Istituto Botanico of the University of Rome. The results of this study on ten species of the families Papaveraceae and Fumariaceae are summarized in Table 1.

The extracts were prepared by finely chopping 20–30 g of fresh roots, pounding them in a ceramic mortar and gradually adding 200 ml. of absolute alcohol. After filtering, the extracts were kept in tightly stoppered bottles until use. The cytological material used consisted of actively growing root tips of *Vicia faba*, *Tulbaghia alliacea*, *Allium pulchellum*, and of human material including buccal smears and chromosome preparations from the cultured cells. The preparations were made by the technique described by Vosa³ for quinacrine fluorescence. The fluorescent substances present in all the extracts showed great affinity for the nuclei and the chromosomes of the tested material, with very little or no cytoplasmic fluorescence.

In *Chelidonium majus*, *Macleaya cordata* and *Glacium flavum*, the fluorescence obtained approached the intensity of that of

Table 1

Staining extracts	Y-body	Specimen <i>Vicia faba</i>	<i>Allium pulchellum</i>	<i>Tulbaghia alliacea</i>	Fluorescence intensity	Fluorescence of solution
<i>Papaver somniferum</i>	visible	+	+	+	**	orange-red
<i>Papaver rhoeas</i>	visible	+	+	+	**	orange-red
<i>Macleaya cordata</i>	visible	+	+	+	***	orange
<i>Chelidonium majus</i>	visible	+	+	+	***	orange
<i>Glacium flavum</i>	visible	+	+	+	***	pale orange
<i>Argemone grandiflora</i>	—	+	+	+	*	pale yellow
<i>Platystemon californicum</i>	—	+	+	+	*	none
<i>Eschscholtzia lobbii</i>	—	+	+	+	*	none
<i>Fumaria officinalis</i> †	—	+	+	+	*	none
<i>Corydalis lutea</i> †	—	+	+	+	*	none

†Fumariaceae; —, Y-body not visible; +, quinacrine-like bands present; fluorescence intensity: *** high, ** medium, * low.

yellowish fluorescence of low intensity. They were barely useful for detecting the banding patterns in most plant chromosomes, and did not give good results in human material owing probably to the low concentration of the fluorescent substance present.

Apart from differences in the intensity of the fluorescence, most of the plant extracts tested gave essentially the same banding patterns as quinacrine. They possess the same characteristic property of discriminating between the different kinds of heterochromatin, and the fluorescent substances they contain may therefore be in some way structurally equivalent. All the species of the Papaveraceae contain isoquinoline alkaloids, which are well known in *Papaver somniferum* and *Chelidonium majus*. The basic chemical structure of quinacrine with its quinoline ring is in fact very similar to those of these alkaloids. The mutagenic and anti-neoplastic effects possessed by quinacrine⁴⁻⁶ are similar to those of certain alkaloids found in *Chelidonium majus* and most other Papaveraceae⁷. Besides the obvious interest of the discovery of quinacrine-like substances in the plant kingdom and their possible use in the study of chromosome structure, this investigation reveals their specificity for certain chromosome segments, and may lead to an understanding of the mechanism of drug-induced chromosome damage.

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C. G. VOSA

Botany School,
University of Oxford

G. D'AMATO
R. CAPINERI
P. MARCHI
G. DE DOMINICIS

Istituto Botanico dell' Università,
Rome

Received July 6, 1972.

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Food-sharing Behaviour within a Group of Douc Monkeys (*Pygathrix nemaeus nemaeus*)

ALTHOUGH food sharing has been observed among gibbons¹, the active donation of food by one non-human primate to another has been reported only for free ranging chimpanzees^{2,3}, and—in a single case—for captive gorillas⁴. Such behaviour has not been reported for monkeys. In the absence of positive evidence, it has seemed reasonable to assume that monkeys do not share food, except in the sense of feeding in close proximity to one another⁵. Since the active sharing of food may have been of fundamental importance in the early evolution of mankind⁶⁻⁸, examples of such behaviour among non-human primates are of particular interest to anthropologists. I describe here some observations of food sharing and donation in a captive group of douc monkeys (*Pygathrix nemaeus nemaeus*).

A group of six doucs, kept in a large outdoor cage at the

San Diego Zoo, were observed for 200 h during June, July and August 1971. One hundred of those hours were devoted to the quantitative scoring of behaviour. (A complete report of this work, including an ethogram of the animals, is in preparation.) The group consisted of one adult, *M*, three adult females, *F1*, *F2* and *F3*, one juvenile male, *J*, and one infant female, *I*.

Each morning, as a regular part of their diet, the doucs were supplied with as much *Eugenia*, in the form of leafy branches, as their keepers expected them to eat during the day. If they ate it all, more was usually supplied.

The behaviour of the monkeys in relation to their eating of the *Eugenia* was observed to be on a continuum from eating alone, through the passive sharing of branches, to the active behaviour of the breaking off and donating of small branches of *Eugenia* to each other. Typically, a douc that was browsing on the *Eugenia* either held the branch in both hands and bit off and ate the leaves and bark, or it held the branch with one hand and used the other to pull off a twig that was then carried up to the mouth for consumption. Quite often, two or more doucs shared the same branch.

Sometimes, two or more monkeys engaged in a tug-of-war over a branch. Usually, in such cases, the result was a stalemate, and the participants settled down and shared the branch until one or the other of them released it—most often when that monkey ceased to feed. At other times, the tug-of-war would be settled by one monkey's biting off a part of the branch and taking that. These contests were normally not accompanied by any aggressive behaviour that was detectable by the observer.

On four occasions, a monkey was observed in the active behaviour of breaking off and giving to another douc a part of a branch. Twice, *F2* broke off a piece of *Eugenia* and handed it to *M*, who then fed on it. On the second occasion, she was sitting on an artificial branch holding some *Eugenia* on which she and her offspring, *J*, had been browsing. *M* arrived beside her on the branch, and—as he did so—she twittered and grimaced (submissive gestures). *M* reached for the branch that *F2* was holding, but she turned away from him so that her body was interposed between *M* and the *Eugenia*. *F2* then bit off a piece of the branch, turned back to *M* and handed it to him. *M* took the offered portion and began to feed on it.

On another occasion, *F1* made what was apparently an unsuccessful grab with her hand at a *Eugenia* branch on which *F3* was feeding. *F3* immediately broke off a piece and allowed *F1* to take it, by holding it within her reach.

In the fourth case, *M* was feeding on a large *Eugenia* branch. *J* reached out with his hand towards the *Eugenia* but did not take hold of it. *M* broke a twig off the main branch and held it within reach of *J* who took it by hand, moved away a few feet, and then settled down to eat it.

Thus active donation was observed between adult females, from adult female to adult male, and from adult male to juvenile male. No begging gestures of the kind exhibited by chimpanzees^{2,3} were observed, although the extremely subtle nature of the communicatory repertoire of the douc makes it possible that some other (unobserved) form of begging took place. The observations cannot be interpreted in terms of food donation as an appeasement gesture. For example, although there was no clear linear hierarchy of dominance among the adults, *M* was never submissive to *J*, yet *M* did donate *Eugenia* to *J*.

These observations were made in unnatural conditions. Yet several researchers who have compared findings from captive and wild examples of the same primate species find no major distortions of behavioural phenomena among the captive specimens¹⁰⁻¹². The sharing and donation of food that were observed among the doucs took place in spite of the ready availability to all of them of alternative leafy branches—as would presumably be the case in the wild.

The observations therefore suggest that active food sharing is possibly an older and more general primate characteristic than was previously believed, and that it is not necessarily

associated with predation, nor with a limited supply of food. Furthermore, it was not necessarily a hunting and gathering way of life that led to altered selection pressures which were the critical factors in the emergence of active sharing behaviour in early man⁹. The alternative, and equally possible, speculation is that active sharing behaviour was a part of our ancestors' repertoire long before the hunting and gathering way of life was adopted.

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MICHAEL KAVANAGH

Department of Psychology,
University of Georgia,
Athens, Georgia 30601

Received June 19, 1972.

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Effect of Humming on Watching Television

RUSHTON has shown that humming causes the eyes to vibrate and this, in turn, produces a stroboscopic effect when a sectorized disk is viewed in steady light¹. He demonstrated this phenomenon by using a black-and-white sectorized disk rotated on a phonographic turntable. When a subject hummed at the correct frequency (determined by the speed of the turntable and the number of sectors on the disk), he saw the sectors standing motionless. Slightly lower and higher pitched hums produced apparent motions of the sectors in the clockwise and counterclockwise directions, respectively.

Although unaware of Rushton's humming effect, one of us (P. C. W.) observed a related phenomenon while watching television. Humming caused the appearance of horizontal lines on the screen. The lines were visible only to the person who was humming. They could be made to stand motionless or to drift upwards or downwards on the screen, depending on the frequency of the hum. Harmonic frequencies generated multiples of the lines and very high frequencies caused a noticeable decrease in line widths.

The effect is most clearly seen if the subject stands well away from the set. This would seem to support Rushton's idea that

the effect is due to the displacement of the image on the retina because the effect of small displacements caused by vibration would be more enhanced the smaller the visual angle being subtended.

The stripes show up as grey and indistinct areas on both black-and-white and colour sets. Apparently some visual information is being encoded for; if it were not, the stripes would probably look black.

We hope that by describing this effect we will help bring Rushton's humming phenomenon within easy test of those who do not have phonographs but who do occasionally watch television.

PHILIP C. WILLIAMS

3105 Ortega Drive,
Tallahassee, Florida 32303

THEODORE P. WILLIAMS

Institute of Molecular Biophysics,
Florida State University,
Tallahassee, Florida 32306

Received July 10, 1972.

- ¹ Rushton, W. A. H., *Nature*, 216, 1173 (1967).

The Fourier Transform of Evoked Responses

INVESTIGATIONS into the relationship between evoked potentials and human intelligence have been carried out by Ertl¹, who claims to have found no evidence to support my earlier conclusion² regarding this relationship. In my opinion, Ertl's work supports my conclusion that there is a significant difference between the evoked potentials for high and low intelligence groups. Although Ertl uses a Fourier analysis rather different from my own analysis, it should be possible to relate the two investigations (see, for example, ref. 3).

I find it necessary to show this relationship by prediction from the results given in my letter because of the difficulties encountered in the frequency domain. According to my work, Ertl's group of high IQ subjects would show a natural resonant frequency of 14 Hz or more, and his low IQ group a frequency of 6 Hz or less. Because the frequencies mentioned in ref. 2 are natural resonant frequencies, it is necessary to

multiply them by a factor $\frac{1}{\sqrt{1-\zeta^2}}$ to shift these frequencies to

the axis along which Ertl has evaluated the transform⁴. My records indicate a considerable variation in the value of the damping factor ζ , but a value of 0.7 would seem to be about average. On performing the necessary calculations, I would expect the apparent frequencies in the Fourier transform to be 19.6 Hz or more, and 8.4 Hz or less. In Fig. 1 (ref. 1), the curve for the high IQ subjects has a peak above the characteristic shape of the transform at 20 Hz and the curve for the low IQ subjects has a peak above the characteristic shape at 8 Hz. Fig. 2 also shows the same frequency components, but the accuracy is lower because of the shorter evaluation period.

It would therefore seem that Ertl's investigation tends to confirm my original findings, rather than disproving them.

W. F. BENNETT

Capilano College,
West Vancouver,
British Columbia

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Kammerer's Midwife

IN his concern with re-delivering Kammerer's work, Koestler has assumed that if Kammerer's experimental integrity were accepted, his Lamarckian conclusions would be reasonable¹, a flaw unnoticed by a recent review². However, known phenomena are sufficient to explain Kammerer's results. Most controversy followed work on the terrestrial midwife toad, eggs from which were immersed in water for several generations. Most eggs died but eventually some male descendants were produced with nuptial pads, characteristic of aquatic anurans. Kammerer suggested acquired inheritance, but intensive selection had occurred and a third explanation is that an environmentally-triggered gene switch had operated.

In Kammerer's other work he confuses adaptation at the individual level with evolutionary adaptation. For example, the European salamander changes its colour in response to background. The change is hormone-induced³ and the salamanders are viviparous, so it is not surprising that at birth young salamanders have the same colouring as their mothers. The factor that is inherited is the ability to change colour; the birth colour is a maternal effect. Superficially the Lamarckian explanation is merely a rather unlikely alternative. Considered further it is even less likely, for there is no model to explain how an acquired character could be incorporated into the genome. If environmentally triggered cellular changes are to direct evolution then either the cell must be able to distinguish *a priori* which changes are beneficial and therefore to be incorporated, or numerous random changes occur with only a few beneficial changes eventually surviving. The former is magic; the latter is a theory uncommonly close in spirit and execution to that of random mutation and natural selection.

J. P. A. ANGSEESING

St Paul's College,
Cheltenham GL50 4AZ

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Faecal Pollution of Our Beaches — How Serious is the Situation?

SMITH¹ determined the incidence of antibiotic resistant coliform bacteria in various rivers, paying particular attention to *Escherichia coli* with transmissible resistance to chloramphenicol; this resistance is potentially dangerous because it may be transferable to *Salmonella typhi* and so render the treatment of typhoid fever more difficult. An important conclusion that emerged from his work was that most of the antibiotic resistant coliforms and R⁺ *E. coli* in rivers examined came from urban sewage. These types were present even in sewage from areas with no abattoirs; human beings were thus shown to be the main source of antibiotic resistant types in the rivers. Smith² subsequently determined the incidence of antibiotic resistant coliforms and R⁺ *E. coli* in coastal bathing waters and reported

that the ratio of the concentrations of the different kinds of antibiotic resistant coliform organisms to each other and to the antibiotic sensitive organisms in the seawater resembled that in human sewage previously examined¹. He concluded² that R⁺ *E. coli* in seawater provided "stronger evidence of contamination with human sewage", and that "the present undesirable situation could be corrected immediately if proper disposal of sewage from seaside towns were practised".

We would like to look further at three aspects of the implications of this work. First, does the presence of R⁺ *E. coli* and other antibiotic resistant coliforms in fact provide "stronger evidence of contamination with human sewage"—presumably as opposed to contamination by animal faeces *via* farm wastes and rural drainage? Second, is there evidence that the situation is undesirable from the public health point of view? Third, what constitutes proper disposal of sewage from seaside towns?

Antibiotic resistant coliforms including *E. coli* are present in animal faeces. Although contamination by animal faeces may be as aesthetically undesirable as contamination by human faeces, it is less dangerous because large numbers of faecal bacteria from an animal would have to be ingested to cause serious illness, while the ingestion of only a few human intestinal pathogenic bacteria can cause disease.

Recent work in America³, where admittedly more animals receive antibiotics than in UK, showed that from 16 to 96% of *E. coli* strains isolated from animals on various farms showed multiple resistance. Smith⁴ found R⁺ *E. coli* in calves, pigs and fowls as well as in human beings, and Walton⁵ isolated strains of *E. coli* showing multiple resistance from the faeces of healthy pigs and calves. Studies such as these suggest there is no *prima facie* evidence for assuming that there are more antibiotic resistant coliforms in human sewage than in rural (i.e. predominantly animal) sewage and surface run-off. Bearing this in mind we recalculated Smith's data¹ to obtain for each antibiotic the resistant coliforms expressed as a percentage of the total coliform count (Tables 1, 2) and concluded that the number of resistant coliforms isolated by Smith had depended more on the total number of coliforms (resistant + sensitive) present in each sample than on the source. Thus the results do not support the idea that counts of antibiotic resistant coliforms and of R⁺ *E. coli* distinguish between contamination from urban sewage and contamination from rural sources; so more work is required.

Our recalculation, although showing that Smith's survey² provides no bacteriological evidence that contamination was from human beings, does not reduce his demonstration of faecal contamination, sometimes heavy and probably from human beings, of several beaches and so we have to consider if there is any scientific evidence that such contamination is dangerous in sea bathing water.

There is no generally accepted bacteriological standard for bathing waters in the UK, not because of apathy, but because a great deal of research by government scientists, local authority health officials and others, has indicated that a reliable standard cannot be formulated. There are two main reasons for this. First, many factors, especially roughness of sea and amount of sunlight, affect the numbers of coliform bacteria recovered on successive days; there may be ten-fold differences⁶. Second, there is no epidemiological evidence that disease is transmitted by sea bathing, except perhaps when the sea contains recognizable faeces. In other words⁷, "The possibility of contracting an enteric disease as a result of bathing in polluted seawater cannot be entirely ruled out. On the other hand, when there are no aesthetic objections the probability of contracting a serious disease by bathing in sewage polluted water is so small as to be epidemiologically undemonstrable".

There remains the possibility that R⁺ *E. coli* may become established in the gut as a result of bathing in sewage polluted water and so be available to transfer their resistance to pathogenic organisms. This possibility seems slight, because large doses are required for transfer to occur⁸, and not particularly important, because many people already carry R⁺ *E. coli*⁹.

Table 1 Data of Smith on Concentration of Antibiotic-resistant Coliform Organisms in Specimens of River Water, Recalculated to Give Resistant Coliforms as a Percentage of Total Coliforms

Origin of specimen	C *	T *	% Coliforms resistant to		Nal *	A *	No. of resistant and sensitive coliforms/ml.
			S *	Neo *			
Tame, after Birmingham	0.6	4	1.6	0.4	0.02	4	5,000
Cole, after Birmingham	0.6	2	1.6	0.3	0.04	8	5,000
Don, after Thorne	1.5	12.5	25	1	2.5	50	800
Ribble, at Preston	0.8	2.5	1.25	0	0.3	12.5	2,000
Groom, at Groomsbridge	0.07	1.33	1	0.03	0	33.3	15,000
Lyme, at Newcastle	0.14	3.25	2	0.05	0	12.5	4,000
Ebbw, at Bassaleg	5	25	25	2	0.5	50	200
Douglas, at Rufford	0.08	2.8	4	0.2	0	32	2,500
Avon, before Bristol	0	0	2.66	0	0	26.6	150
Avon, after Bristol	0.01	0.2	0.27	0.01	0.01	6.67	75,000
Severn, before Stourport	0.3	4	16	0	0	60	50
Severn, after Stourport	0.27	5	7.5	0	0.13	50	800
Stour, at Stourport	0.25	3.5	8	0.15	0.05	30	10,000
Thames, at Westminster	0.1	1.5	1	0	0	25	400
Thames, at Westminster †	0.4	3	3	0	0.1	30	1,000
Great Ouse, before Huntingdon	0	0	0	0	0	0	150
Jed, at Jedburgh	0	0	0	0	0	0	50
Cam, at Cambridge	0	0	6	0	0	40	50
Leader, at Leader	0	0	0	0	0	30	10

* C, Chloramphenicol; T, tetracyclines; S, streptomycin; Neo, neomycin; Nal, nalidixic acid; A, ampicillin.

† Collected in October 1970 during a partial strike of sewage workers.

Original data from ref. 1.

Table 2 Data of Smith on Concentration of Antibiotic-resistant Coliform Organisms in Specimens of Water from River Taff and Tributaries, Recalculated to Give Resistant Coliforms as a Percentage of Total Coliforms

Collection site	*C	T	% Coliforms resistant to		Nal	A	No. of resistant and sensitive coliforms/ml.
			S	Neo			
Before Merthyr Tydvil	0	0	0	0	0	0	0
At Troedyrhiw	0	0	5	—	0	50	20
Before Aberfan	0.1	2	10	0	0	8	50
After Aberfan	1.6	16	8	0.4	0	80	250
After Abercynon	0.25	2.5	5	0.25	0.01	50	20,000
At Cilfynydd	0.33	3.33	5	0.67	0	16.67	3,000
Before Pontypridd	0.13	3.75	5	0.2	0	25	4,000
After Pontypridd	0.1	2	7.5	0.03	0	37.5	4,000
At Upperboat	0.3	5	7	0.3	0	30	1,000
At Taffswell	0.04	0.8	2	0.2	0	10	5,000
At Whitchurch	0.3	6	6	0	0	20	500
At Cardiff Castle	0.04	1.2	4	0	0	20	500
Before Cardiff docks, Tributaries	0.1	4	10	0	0	26.67	150
Rhondda Fawr, before Tynewydd	0	0	0	0	0	0	0
Rhondda Fawr, at Tonypany	0.03	3	1.2	0.1	0	8	1,000
Rhondda Fawr, at Porth	0.03	2.8	8	0.12	0	20	2,500
Rhondda Fawr, at Pontypridd	0.07	2	5.3	0	0	5.3	1,500
Rhondda Fach, before joining Taff	0	0	10	1	0	60	100
Cynon, before joining Taff	0.67	13.33	3.33	0.67	0	13.33	150

* As in Table 1. Original data from ref. 1.

The Jeger Committee¹⁰ recommended that authorization should be required for all coastal discharges because a potential risk to public health exists in the grossly polluted places at present and because there is "to put it mildly a diminution of pleasure". They could not, however, recommend that authorities should demand full conventional treatment of all sewage before discharge to the sea as the cost would not be worth the benefit. So it seems that for small resorts, at least, there is no evidence to justify full treatment of sewage: comminution, which by breaking large particles exposes bacteria to rapid oxidation, irradiation and other inhibitory factors, and discharge from a point chosen to minimize the possibility of return to beaches or damage to shell fisheries and recreational waters should usually be satisfactory. It is unlikely that such treatment will ensure that no faecal *E. coli* will contaminate bathing beaches but it is probably all that is necessary. It seems that if sea bathing waters in UK are not visibly contaminated with faeces then there is no evidence of public health risk. Those who argue for more extensive treatment than this should acknowledge that their case rests on aesthetic rather than scientific grounds. Many British rivers are at least as contaminated as some of the worst beaches; they receive inadequately treated or untreated sewage which kills the animals and plants characteristic of clean rivers and renders the water unfit for consumption without very extensive and hence expensive treatment. We believe that unreasoned concern for coastal waters should not cause money to be spent on provision of plant for excessive treatment of sewage to be discharged into the sea while much of our inland sewage remains inadequately treated or not treated at all.

A. P. REGNIER
R. W. A. PARK

Department of Microbiology,
The University,
London Road,
Reading RG1 5AQ

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Disagreements on Why Brown Pelican Eggs are Thin

I FIND four points of disagreement with the proposal of Blus *et al.*^{1,2} that DDE is the probable cause of thin eggshells in brown pelicans.

First, his Fig. 1 is based on data points of residue and shell thickness for three separate colonies composed of two sub-species. If this overall correlation is meaningful, each colony should show a similar trend in itself, which is not the case. None of the separate colonies shows a clear trend in itself.

Second, within the lines for 95% confidence limits in Fig. 1, it is possible to have a series of shell measurements parallel to the abscissa. In other words, his 95% confidence limit could include a series of eggs with residues extending from none to a

maximum, with no change in shell thickness. This suggests extremely variable supporting values for the regression.

Third, whole egg analysis is inappropriate for incubated eggs because the residues are found in the yolk, and during incubation yolk contents including residues are subject to metabolic changes. I show below that DDE residues are metabolized as brown pelican eggs are incubated. It is not possible to determine the extent of incubation of Blus's eggs from the published literature, but a table was presented at the public hearing on DDT (Exhibit R-74) which shows that Blus's South Carolina and Florida eggs contained embryos; two were even "heard peeping".

Fourth, the use of Pearson's product moment correlation coefficient (*r*) is not an appropriate method for values which are not bi-variantly normally distributed. Using logarithms for residue levels shows that residues are not normally distributed around a mean value. Non-parametric statistics should be used³.

To understand that Blus's claims about pelican eggs and residues may not be correct, we need to look at some unpublished analyses provided by G. R. Arnett, director of the California Department of Fish and Game (CDFG). These findings were from eggs collected on Anacapa Island off the California coast. Four of these eggs were part of 25, collected on April 18, 1969 (ref. 4). Mr Blus's sample of 10 was from the same collection (11 eggs are not accounted for). A sample of May 27, 1969, represents eggs taken when adults were shot off their nests on Anacapa Island by State and Federal researchers⁵. The female with the higher residue of DDE had the thicker shelled egg of the two females collected.

The data of Table 1 show the following points. 1, Lipid levels in the yolk drop nearly ten-fold during incubation (26.9 to 2.8%). 2, Yolk plus embryo weight increases about three-fold (13.6 to 49.7 g) during incubation. 3, Whole egg residues of DDE seem to fit a similar ten-fold level of decrease with incubation (357.5 to 29.4 p.p.m.). 4, Whole egg DDE residues in variously incubated eggs therefore should not be expected to correlate with shell thickness, even if a correlation existed in newly laid eggs.

Dr E. H. Dustman (personal communication) supplied the data used to establish the points in Fig. 1 of Blus's paper¹. These data had one obvious typographical error for Anacapa Island, which was corrected. Using Blus's data and those from Table 1, Spearman's rank values were calculated⁶ for brown pelican eggs (Table 2).

From these data, I conclude that the statement of Blus *et al.*¹, "A concentration-effect relationship seems to exist between DDE in eggs and shell thinning", is correct, but not in the way Blus *et al.* intended. Whole egg residues of incubated eggs seem to be valueless in determining a cause and effect relationship. The CDFG data (Table 1) show a nearly perfect correlation of lipid DDE residues to shell thickness, and the relationship is positive. Even though thicker shells are associated with higher residues, I do not believe that DDE causes shell thickening in brown pelican eggs. The data appear to completely refute that DDE causes thinning of pelican eggs. If DDE were causally related to shell thinning, it would be correlated in every sample and other factors should be investigated to find the cause of the thin shelled eggs observed in this species.

Blus *et al.* mention peregrine falcon egg residues, suggesting that cause and effect studies were conducted with this species. Arguments for the cause of collapse in peregrine falcon populations in the Arctic may⁸ suffer from the same problems as the work of Blus *et al.* Three populations of varying reproductive success are considered together, unidentified, and whole egg DDE residues are used to determine a regression coefficient (*r*) for residues correlated to eggshell values. There is no mention of stage of embryo development, lipid level or which of the three populations provide the points in the figure showing the regression line. There are further problems of non-uniform methods of egg content preservation used in this study. More important is evidence that the available eggs were as thin in

Table 1 Anacapa Island (California) Brown Pelican Egg Data, supplied by the California Department of Fish and Game

Date collected	Weight yolk (g)	% lipid in yolk	Shell thickness (mm)	Incubated	Residues in $\mu\text{g/g}$ of sample (p.p.m. whole yolk)					Calculated p,p'DDE lipid basis (p.p.m.)
					p,p'DDE	p,p'DDMU	p,p'DDD	p,p'DDT	o,p'DDT	
18/4/69	15.1	21.8	0.42	no	357.5	20.9	8.3	6.9	4.3	1,640
	38.7	6.3	0.38	yes	61.1	4.1	1.6	2.0	1.2	970
	15.3	23.7	0.37	no	204.4	20.3	11.4	10.5	5.0	860
	17.5	22.9	0.37	no	232.1	30.3	17.2	14.7	10.5	1,010
27/5/69	13.6	26.2	0.36	no	178.4	13.0	8.9	7.5	—	680
	16.8	26.9	0.34	no	183.0	13.4	9.1	8.9	—	680
	47.9	4.4	0.40	yes	55.8	2.4	1.1	1.4	—	1,270
	25.3	12.2	0.40	yes	143.4	7.4	3.0	2.9	—	1,172
	49.7	2.8	0.38	yes	29.4	3.3	2.2	1.7	—	1,045

Eggs submitted for analysis by James Keith, US Department of Interior, Bureau of Sport, Fishery and Wildlife.

1952 and 1964 as they were in 1970 when the alleged collapse occurred. Scientific persecution appears to be just as viable a hypothesis as DDE or other causes for problems of reproduction failure in these northern peregrine populations.

Table 2 Spearman's Rank Values for Blus's and Arnett's DataWhole egg DDE $\times$ shell thickness

Blus's data, South Carolina, $n=21$, $r_s = -0.0964$ NS

Blus's data, Anacapa Is., $n=10$, $r_s = +0.1454$ NS (thickest shells $\times$ highest DDE)
 $r_s = +0.393$ NS (thinnest shells $\times$ highest DDE)

CDFG, Anacapa Is., $n=9$, $r_s = +0.4771$ NS

Blus+CDFG, Anacapa Is., $n=19$, $r_s = -0.0548$ NS

Lipid basis DDE $\times$ shell thickness

CDFG, Anacapa Is., $n=9$, $r_s = +0.9834$ highly significant, nearly perfect (as residues increased, shells were thicker)

Table 3 Spearman's Rank Values from Risebrough's DataLipid basis residue $\times$ shell thickness, Anacapa Is.,

DDE; $n=65$, $r_s = -0.4318$ highly significant

PCB; $n=65$, $r_s = -0.1361$ NS

Risebrough gives r values for DDE as -0.5605 (Sig <0.001) and PCB as -0.2527 (Sig <0.05).

In order to check further, the lipid residues given by Risebrough⁷ for Anacapa Island eggs were evaluated by Spearman's rank (Table 3).

The data necessary to arrive at an understanding of pesticide residue levels, rapid residue loss rates in eggs with incubation,

metabolism of lipids and other pertinent factors should have been published, along with the original contentions and conclusions. That DDE is the cause of thin brown pelican or peregrine eggs is well established in the popular press and scientific literature, but the underlying data to test the conclusion are just now becoming available and do not support such a conclusion. This is reason for concern about actions to ban pesticides based on these faulty conclusions. There is no place in science for suppressed conflicting data, or an "end justifies the means" philosophy. Scientists can be responsible agents for change only when they consider and present all the available data which bear on their conclusion.

WILLIAM HAZELTINE

26 Rosita Way,
Oroville, California 95965

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BHC Not Found to Reduce the Shell Quality of Hens' Eggs

SEVERAL organochloride pesticides are said to have detrimental effects on the eggshell quality of a variety of avian species. The eggshell thickness of ducks is reduced by feeding dieldrin and DDE^{1,2}; that of American kestrels by DDE³; of Japanese quail by DDT⁴ and of American sparrow hawks by a mixture of DDT and dieldrin⁵. Indeed, a mathematical relationship seems to exist between DDE residues and shell thinning⁶. Major

structural defects, apart from shell thinning, have also been found to occur in the eggshells of quail fed DDT or chlordecone⁷. Now that the use of DDT has been, or is about to be, banned in many parts of the world, γ -BHC (lindane) is becoming the most widely used pesticide in this class. However, little is known about its effects on birds. Whitehead *et al.*⁸ found that feeding γ -BHC at moderate levels (about 100 mg/kg diet) to hens permanently reduced their egg production by 25%, although no detrimental effect was observed on shell thickness. In contrast, Sauter and Steele⁹ have claimed that feeding it to hens at a lower level, 10 mg/kg diet, slightly reduced shell thickness.

To investigate the effect of γ -BHC on several aspects of shell quality this pesticide was fed to laying hens at levels equivalent to 10, 100 and 200 mg/kg diet. Effects on the thickness, calcification, strength and structure of their eggs were studied. Forty-eight 15-month-old laying hens were housed in individual wire cages and given unrestricted access to water and a commercial layers' ration containing 3.4% calcium. Measurements of shell thickness, shell shearing strength and percentage shell calcium were made on eggs from each bird, and cross-sections of shells were examined by scanning electron microscopy. Twelve birds were then allocated at random to each of 4 groups. Birds in groups 2, 3 and 4 were given daily doses of 1.25, 12.5 and 25.0 mg γ -BHC, equivalent to approximately 10, 100 and 200 mg/kg diet, in gelatine capsules. Group 1 was used as a control. After allowing the birds one month in which to equilibrate with the treatments, observations on the eggs were repeated.

Table 1 Egg Production, Shell Thickness and Shell Calcium Content of Hens before and during Treatment with γ -BHC

Group	Period	% Egg production (hen-day basis)	Mean shell thickness (μ m) $\pm$ s.e.	Shell calcium (% of whole egg) $\pm$ s.e.	% Decrease in shell Ca
1	1	58.9	299 $\pm$ 2.2	3.111 $\pm$ 0.083	5.01
1	2	56.3	295 $\pm$ 2.2	2.955 $\pm$ 0.074	
2	1	61.3	322 $\pm$ 2.3	3.316 $\pm$ 0.102	5.06
2	2	55.7	317 $\pm$ 2.1	3.148 $\pm$ 0.091	
3	1	49.8	311 $\pm$ 2.1	3.266 $\pm$ 0.093	4.84
3	2	34.8	308 $\pm$ 2.0	3.108 $\pm$ 0.098	
4	1	58.0	323 $\pm$ 2.3	3.270 $\pm$ 0.110	4.28
4	2	41.0	325 $\pm$ 2.5	3.131 $\pm$ 0.082	

Period 1: Prior to treatment.

Period 2: Period during which birds in groups 2, 3 and 4 received 1.25, 12.5 and 25.0 mg γ -BHC each day.

Shell thickness was measured, using a micrometer screw gauge with a rounded anvil, at 3 positions around the equator after removal of the membranes. Calcium was determined by atomic absorption spectrophotometry of solutions obtained by dissolving shells in concentrated hydrochloric acid. A Cambridge 'Stereoscan' scanning electron microscope was used to examine gold-coated sections of shell. These were examined with membranes present and again after the membranes had been removed following treatment for 1 h with 5% EDTA (pH 8.5). Measurements of shell shearing strength were made with the apparatus described by Carter¹⁰. Mean force at failure, Y , was plotted against mean shell thickness, X , and the slope of the relationship between Y and X was calculated as $\sqrt{b_1/b_2}$ where b_1 is the coefficient of regression of Y on X and b_2 is that of X on Y . The slope measures the strength per unit thickness of the outer ("spongy") layers of the shell. The intercept on the X -axis of the line of this slope passing through the mean of the distribution shows the thickness of the weak

mammillary layer at the inside of the shell that contributes little to its shearing strength¹⁰.

The egg production data (Table 1) show that during the treatment period the rates of production of groups 1, 2, 3 and 4 were reduced by 4.3, 9.1, 30.1 and 29.3% respectively compared with the rates prior to treatment. The decrease in production for group 3 was similar to that previously reported for hens fed γ -BHC at this dose rate⁸.

The shell thickness values each of which represents the mean of between 150 and 200 observations did not show any significant effects of the treatments. Shell calcium expressed as a percentage of egg weight decreased to a similar extent in all groups during the experiment. There was no effect of position in clutch on shell thickness or the calcium content after any treatment. The data for the shell strength measurements are given in Table 2. The treatments had no significant effect on the slope of the relationship of Y with X , indicating that the shearing strength per unit thickness of shell was unaffected, nor was there any significant effect on the intercept.

Table 2 Relationship of Mean Force at Failure to Mean Thickness of Eggshells of Treated and Untreated Birds

Group	Period*	Mean shell thickness, X (μ m)	Mean force at failure, Y (kg wt)	Slope and s.e. (g wt/ μ m)	X intercept (μ m)
1	1	304.6	1.037	4.22 $\pm$ 0.294	58.5
1	2	296.8	0.962	4.23 $\pm$ 0.359	74.6
2	1	309.2	1.040	3.97 $\pm$ 0.386	46.7
2	2	316.2	1.031	4.04 $\pm$ 0.318	59.6
3	1	328.4	1.136	3.97 $\pm$ 0.408	42.3
3	2	314.5	1.087	4.12 $\pm$ 0.395	51.2
4	1	330.6	1.125	4.66 $\pm$ 0.285	89.3
4	2	336.0	1.151	4.56 $\pm$ 0.353	83.2

*As for Table 1.

Scanning electron microscopy disclosed no abnormalities in the shells of groups 2, 3 and 4.

These results demonstrate that although an intake of γ -BHC of up to the equivalent of 200 mg/kg food will reduce the rate of egg production, it does not have a deleterious effect on the eggshells of hens fed a diet containing an adequate amount of calcium.

We thank J. Goodall and M. Maxwell for assistance with the scanning electron microscopy.

C. C. WHITEHEAD
J. N. DOWNE
JOHANNE A. PHILLIPS

Agricultural Research Council Poultry Research Centre,
West Mains Road, Edinburgh EH9 3JS

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BOOK REVIEWS

Human Heredity

The Genetics of Human Populations. By L. L. Cavalli-Sforza and W. F. Bodmer. Pp. xvi+965. (W. H. Freeman: San Francisco and Reading, November 1971.) £10.

THE rapidly emerging concepts and methodology of current genetic inquiry have tended to polarize its associated literature into highly specialized texts (usually of multiple authorship) requiring a depth of biochemical and/or mathematical preparation which, for ordinary scientific minds at least, is increasingly incompatible with a true understanding of the implications of genetics for human society.

This scholarly two-author textbook is written with the intention of providing a comprehensive and understandable treatment of the genetics of human populations for a relatively divergent and unsophisticated audience of biological scientists. The consistency of its organization and the clarity of its content provide adequate confirmation of the attainment of their goal. It is probably the most complete and definitive reference available today. Certainly it is remarkable that so wide a field as human heredity could be encompassed in such detail.

In a textbook as extensive as this (965 pages) it was surprising to find so few minor imperfections. Misspelled words, improperly labelled figures and other similar plagues besetting the text writer are rare. Thus, an impression of careful attention to detail is created along with the associated implication of similar patient endeavour in the formulation of the information content.

The twelve chapters are diverse in their subject matter and, although the juxtaposition of data is sometimes startling, it usually is illuminating, especially in the discussion of mechanisms whereby genotypic effects are expressed in the phenotype.

Considerable personal, and to my knowledge, unpublished data have been integrated by the authors in appropriate sections of the text. Summary sen-

tences and intelligently structured and "worked example" problems provide a unique device for maintaining interest. I found the chapters on "Transient and Balanced Polymorphism", "Polymorphisms for Blood Groups, Transplantation Antigens and Serum Proteins: Incompatibility Selection", "Genetic Demography and Natural Selection", and "Population Structure" exceptional.

Although data from a variety of disciplines are used, no unduly specialized knowledge seems required. The "general" reader, however, may be thwarted by the complexity of the algebraic expressions, should he choose to follow the solution of worked examples which conclude several of the chapters.

The final section of the book includes three appendices. Appendix 1 is a limited introduction to the elements of statistics and probability, and was the source of my only unfavourable impression. I can best define it as excess baggage. Surely, the average reader will already have mastered statistical theory and methodology at this level of presentation.

Appendix 2 is a stimulating and unique condensation of newer approaches to segregation and linkage analysis in human pedigrees and the estimation of gene frequencies. With the addition of substantive material, it could be quickly expanded into a valuable independent text.

Appendix 3 consists of eighty-one questions taken from a final examination at Stanford University. I would challenge all who consider this text from the perspective of ascertaining its relevance to their current degree of genetic sophistication to undertake first self-evaluation by use of the examination questions.

In short, I can honestly state that this is a fine book. It was a pleasure to read it and to enjoy it as a stimulating companion. The tables, charts, and graphs are readily understood and additive to the value of the written component. The subject matter provides a balanced interaction of mathematical theory and

empirical information. I would not hesitate to recommend it highly to anyone seeking an integrated understanding of human population genetics.

H. TURNER

Irradiated Water

The Radiation Chemistry of Water. By I. G. Draganic and Z. D. Draganic. Vol. 26. Pp. xi+242. (Academic: New York and London, 1971.) \$14; £6.55.

THIS monograph may be considered as a follow-up to A. O. Allen's classic book *The Radiation Chemistry of Water and Aqueous Solutions* (1961). The eight chapters cover the history, primary processes, reducing radicals, oxidizing radicals, radical yields, diffusion kinetic models, techniques and dosimetry.

Overall the book is a relatively compact assessment of the radiation chemistry of aqueous solutions in which the presentation of the data is ordered so as to emphasize the fundamental processes occurring in irradiated water. Each chapter is preceded by a short summary, an excellent idea that could well be used more generally. The authors' treatment of the history of the subject has a certain personal flavour but not so much so that it will be too unpalatable to the majority of those in the field. As a general introduction to the subject for students and those seeking background knowledge I would recommend this book as an adequate, clear and well produced volume. When one considers this as a specialized textbook in physical chemistry, however, its drawbacks are more serious. Radiation chemistry ceased to be an end in itself some time ago and its potential as an investigative tool in most branches of chemistry is being realized increasingly by those in the field. Appreciation of just what radiation chemistry techniques can do is, unfortunately, not so widespread outside the field and it is in covering this area

that the book falls short. The contributions of pulse radiolysis to reaction kinetics and electron transfer reactions are not brought out and discussed in relation to rate theory. The potential of the method in physical inorganic chemistry is similarly ignored. The high degree of specificity of systems that, when irradiated, will produce a single radical species, for example OH, H or e^-_{aq} , the reactions of which can then be studied, in many cases directly, is an important aspect of contemporary radiation chemistry when viewed in the wider context of physical chemistry.

The authors can also be somewhat uncritical, for example their belief that OH rate constant data obtained by thiocyanate competition are "practically of no use" is not a balanced judgment and unjustifiably condemns a great deal of useful data.

In conclusion, although this book is a useful introductory volume to the subject it does not assess the achievements and potential of radiation chemistry in relation to physical chemistry sufficiently well.

E. M. FIELDEN

Lunar Temperature

Thermal Characteristics of the Moon. Edited by John W. Lucas. Pp. xiii+340. (MIT: Cambridge, Massachusetts, and London, 1972.) \$14.95.

THROUGH this volume, leading investigators in different disciplines have combined to survey the temperatures and physical properties of the surface and interior of the Moon. Their accounts relate essentially to the achievements of the past decade—from pre-Ranger times through the present epoch of continuing spaceflight exploration of the Moon—and have been organized under four broad headings: measurements made from the Earth (82 pages); those made on the Moon itself (94 pages); those made on simulated lunar (or lunar-like) materials (56 pages); and the possible thermal history of the Moon (38 pages).

The overall subject matter of a book such as this might well have been drawn from some conference; this work, however, is much better organized and balanced than the average conference presentation. Each author has tended to give a fair review—frequently with a summary—of his subject, rather than to argue strongly for his particular point of view. Inevitably, therefore, much of the content is of old material—a bias which, taken together with the hindsight and caution which enter the various accounts and punctuated in the light of recent advances by the expert authors themselves, is wholly desirable.

Both lunar specialists and scientists in other fields are likely to benefit from

this book. It is quite well written; it collects together previously detached arguments apposite to the general lunar thermal problem; and it brings the subject right up to date with a brief account of the puzzlingly high heat flow from within the Moon recorded by the thermal probes inserted in the lunar soil, near to the Hadley Rille, by the Apollo 15 astronauts. Neither the immediate difficulties in explaining this high heat flux—nor the importance of the results—were lessened by the failure of the similar experiment set up by the Apollo 16 team.

G. FIELDER

Flora of North America

The Genera of North American Plants. By Thomas Nuttall. Introduction by J. Ewan. Vol. 1. Pp. xxxvii+vii+312. Vol. 2. Pp. 254+10. Facsimile of the 1818 edition. *Classica Botanica Americana*, Vol. 7. (Hafner: New York, 1971.) £14.65.

Flora of the Prairies and Plains of Central North America. By Per Axel Rydberg. Vol. 1. Pp. 1–504. Vol. 2. Pp. 505–969. Facsimile of the 1932, 1 volume, edition. (Dover: New York; Constable: London, April 1972.) \$5; £2.50 each volume.

It is unfortunate for the modern botanist that the present boom in antiquarian book prices is offset by ambitious reprint programmes from certain publishers. Hafner's *Classica Botanica Americana* series provides a good example of a systematic approach to the provision of durable reprints of rare, expensive, and often fragile classics. When such reprints are enriched by the inclusion of a scholarly apparatus like Ewan's introduction to Nuttall the exercise becomes doubly worth while.

Nuttall, a Yorkshireman, emigrated to America in 1808 and soon took to botany under the influence of Benjamin Smith Barton. His *Genera*, published a decade later, provided a masterly conspectus of contemporary knowledge on the North American flora. Written in English and following the Linnaean system it was of immediate value to the botanical student and amateur. Furthermore, Nuttall's wide travels resulted in a breadth of knowledge that made the *Genera* a valuable foundation for later floras. Professor Ewan's excellent introduction provides information on the author, his travels, collections, researches and influence as well as the taxonomic value of the *Genera* for the modern botanist. In addition, there is a useful gazetteer of place names and a clarification of literature references used in the text.

Rydberg, like Nuttall, emigrated to America (from Sweden) at the age of

22. He also travelled very widely and took to writing large scale floras of which the present was his last. This concise work, well provided with keys and illustrations, treats of 1,066 genera (3,988 spp.) compared with Nuttall's 834. Though still in considerable demand this 40-year-old flora would have benefited from a new introduction commenting on its practical and taxonomic worth to the modern botanist. An otherwise utilitarian reprint suffers from division into two volumes which must hamper use in the field.

G. D. R. BRIDSON

Connective Tissue

Journal of Connective Tissue Research. Editor-in-chief, Ines Mandl. Vol. 1. No. 1. (Gordon and Breach: New York, London and Paris, March 1972.) Personal subscription, £5.50 per volume. Libraries, institutions, etc., £15.50 per volume.

WE read after the foreword to this new journal that when an eminent researcher on the subject first heard of it his reaction was unprintable. His mature consideration was that it was not a bad idea. I also find myself with both types of reaction but only time will tell whether the second is appropriate. The familiar problem is raised of whether journals should be according to the subject investigated or according to the method used. Both subject and method are specialities, both require the interaction of specialists to flourish, so probably both types of journal are equally useful. Connective tissue research is a wider field than some already supporting journals. So far, so good. When we examine this issue there are further promising signs. There could not be a better board assembled to administer a journal in this subject and there are a number of significant papers in the first issue. At the level of molecular interaction there is a paper on one of the polymorphic aggregates of the tropocollagen molecule and another which reports that a polymorphic form usually considered artificial is observed *in vivo*. The nature of the intermolecular forces is investigated by new methods of solubilizing collagen and there are two papers on the intermolecular cross-links. Two papers are included on elastin, one of which reports that under the scanning electron microscope this material appears to be composed of fibres embedded in an amorphous matrix. Further topics dealt with are cartilage, basement membrane and the collagen of cornea.

It is obvious that this issue is good and this journal is suitable as a repository for reports on connective tissue research in the future. Whether

or not it succeeds depends on the connective tissue community. Will the methods journals seem even more appropriate or is connective tissue research already sufficiently served by the wider subject journals of biochemistry and molecular biology? This new journal will only be really worthwhile if by reading it one can be assured of covering a large fraction of papers on its topic.

ANDREW MILLER

Poisons

Microbial Toxins. Edited by G. Weinbaum, S. Kadis and S. J. Ajl. Vol. IV. *Bacterial Endotoxins.* Pp. xviii+473. (Academic: New York and London, 1971.) \$26.00.

Microbial Toxins. Edited by S. Kadis, G. Weinbaum and S. J. Ajl. Vol. V. *Bacterial Endotoxins.* Pp. xviii+507. (Academic: New York and London, June 1971.) \$27; £12.60.

Microbial Toxins. Edited by A. Ciegler, S. Kadis and S. J. Ajl. Vol. VI. *Fungal Toxins.* Pp. xxiii+563. (Academic: New York and London, November 1971.) \$29; £13.55.

Microbial Toxins. Edited by S. Kadis, A. Ciegler and S. J. Ajl. Vol. VII. *Algal and Fungal Toxins.* Pp. xvii+401. (Academic: New York and London, December 1971.) \$22; £10.25.

Toxins of Animal and Plant Origin. Edited by A. de Vries and E. Kochva. Vol. 1. Pp. 489. (Gordon and Breach: New York, London and Paris, 1971.) £11.45.

Pharmacology and Toxicology of Naturally Occurring Toxins. Section Editor: H. Raskova. (International Encyclopedia of Pharmacology and Therapeutics. Section 71. Vol. 2.) Pp. ix+299. (Pergamon: Oxford and New York, January 1972.) £6.

AN investment (and such it is) of some £66 brings over 2,700 pages on these various toxins. The literary indigestion of reading them all was shared between Drs D. C. Ellwood, K. D. Macdonald, K. Sargeant and G. Thomas of the Microbiological Research Establishment, and it is their views which are summarized in this report.

The first (IV) of the volumes, *Microbial Toxins*, begins properly with a definition and brief historical introduction to the chemical, biochemical and genetic aspects of microbial endotoxins. Their relationship to the structure of the wall of Gram-negative bacteria is discussed next, followed by a chapter on their physical properties. The preparations so far obtained are heterogeneous, so attempts to understand them, for example in relation to phage attachment in Gram-negative organisms,

result in more unanswered, than answered, questions. The chemistry is unusual also in that they contain a wide variety of different sugars which account for immunological specificity. Biosynthesis and the relation of structure to genetics are also investigated. New advances in an intriguing area are well covered.

The diverse effects of endotoxins on animals are comprehensively reviewed in volume V. The first chapter starts with circumstantial evidence for their relationship to virulence and this leads to a consideration of immunological cross-reaction between blood group and Forssman antigens and the O-antigens of Gram-negative bacteria. The different biological activities are probably referable to different sections of the macromolecules. Endotoxins interact with the complement system, and affect metabolism and the vascular system. These considerations underlie the role of endotoxins in susceptibility to infections, and of the animal's tolerance and hypersensitivity to the toxins themselves.

All the recent work is brought together in these interesting volumes. They give a clear indication of future trends, and even consider the purpose of the toxins from the point of view of the bacteria themselves.

Volume VI is the first attempt to collect together all the data on *Aspergillus* and *Penicillium* toxins. The longest chapter emphasizes the great impetus given to fungal toxin discovery by the emergence of the aflatoxins (from *Aspergillus*) during the last decade. This section discusses toxin-producing fungi, affected foodstuffs, and so on, factors affecting toxin production, analytical methods, safety, biosynthesis, pharmacology and toxicology, and molecular biochemistry, and ends with a short section on the related sterigmatocystin. The remarkable sensitivity of the fluorescence assays for the aflatoxins has led to their detection in many different foods, but the significance of this has still to be evaluated and their possible role as carcinogens for man remains speculative. It is too early, in fact, for the formulation of a policy. This excellent summary has twenty-four pages of references.

The remaining seven chapters of a most useful reference book describe other toxins, including those from yellowed rice, the ochratoxins, the rubratoxins, and cyclopiasonic acid.

The lethal and hallucinogenic effects which follow the ingestion of certain fungi were probably known in prehistoric times and the possibility of a relationship between fungal contamination of food and disease syndromes in man and animals has been suggested since the beginning of the nineteenth century.

The first of seven articles on fungal toxins in volume VII is concerned with zearalenone isolated from *Fusarium graminearum* and discusses the biosynthesis and biological activity of this oestrogenic mycotoxin. Alimentary toxic aleukia, prevalent in some areas of Russia during the Second World War, and with a high human mortality rate, was attributed to toxins from *Fusarium* spp. infected grain left in fields over winter. Scerpene metabolites may be responsible for alimentary toxic aleukia and these may also be carcinogenic. Toxins produced by *Fusarium* spp. which infect fescue grasses are also proposed as the cause of "fescue foot" in cattle grazing on such pastures.

Some of the 12,13-epoxytrichothecenes are cytostatic but their high toxicity probably precludes their use as anti-tumour agents. Excessive salivation and other symptoms in ruminants were related to infection of red clover with the fungus *Rhizoctonia leguminicola* and led to the isolation of slaframine, a piperidine alkaloid, which acts as a cholinergic compound. The chemistry and toxicology of a group of fungal metabolites, the epipolythiodioxopiperazines, are also reviewed.

The three chapters dealing with algal toxins are concerned with those produced by dinoflagellates, blue-green and green algae and species of Chrysophyceae, particularly *Prymnesium parvum*. The chemical structure of most algal toxins remains to be elucidated, but that of a toxin from a species of *Anabaena*, a blue-green alga, has been determined.

Toxins of Animal and Plant Origin, volume 1, is the first of three volumes presenting the proceedings of the Second International Symposium on Animal and Plant Toxins held at Tel-Aviv, Israel, in February 1970. The first, and smallest, of three sections includes reports on the distribution of venomous snakes in Israel and on the methods of locomotion of vipers. The second section describes the structure of viper venom organs, rabbitfishes, the black widow spider and different aspects of venom secretion. The third and longest section, of nineteen papers, is devoted to the biochemistry of snake venoms. Most of these contain phospholipase A, which splits phospholipids into fatty acids and the lysophospholipids which exhibit haemolytic activity. Phospholipase A may also have other pharmacological properties not attributable to its enzymatic function. Basic polypeptides from cobra venom are haemolytic in the absence of phospholipids and can act synergistically with phospholipase A. The two lethal factors of cobra venom are possibly glycopeptides, but one paper indicates that cobrotoxin from the Formosan cobra is a single chain peptide consisting

of sixty-two residues. Its amino-acid sequence has been determined and its toxicity is dependent on the integrity of four disulphide cross-links. Neurotoxins from sea snakes and the Cape cobra are apparently related in structure to cobrotoxin.

This volume should be a useful addition to the shelves of those interested in cellular and molecular developments in this specific area of research.

The chief section of *Pharmacology and Toxicology of Naturally Occurring Toxins* (which is one in an extensive series) is devoted to toxins from marine organisms, from "red blooms" to sting rays, and the therapeutic problems arising from these are extensively discussed. The venoms of insects and arachnida, from honey bees to scorpions, constitute an astonishing variety of toxic agents and symptoms, but these are reviewed in less detail. The section on mycotoxins is also short, but such a deficiency is more than made up elsewhere (*Microbial Toxins*, volume VI, v. *supra*). Although the three groups of toxins are described by different authors with differing styles the book is very easy to read and is supplemented by extensive lists of references. R. J. C. HARRIS

The Dioscoreaceae

Anatomy of the Monocotyledons. VI. Dioscoreales. By E. S. Ayensu. Edited by C. R. Metcalfe. Pp. xii+182+16 plates. (Clarendon: Oxford; Oxford University: London, March 1972.) £6.

OF the volumes in this important series on the anatomy of the monocotyledons, two have been written by Dr Metcalfe, and all the others have been edited and inspired by him. The volume under review, by Dr Ayensu of the Smithsonian Institution, is a worthy member of the series; it deals with an order with many climbing plants, which is distinctive in structure and which is also of economic importance, containing as it does the cultivated yam. Recently, too, a precursor of cortisone and of steroidal hormones has been shown to be present in some species of *Dioscorea*.

In Part I, a general account is given of the morphology and anatomy of the order. The account is based on a representative sample of 130 species, belonging to nine genera and four families. There is much to interest the general botanist in this part of the book. It is easy to forget for how short a time and by how few people the families of flowering plants have been studied; and the author reminds us that we still have a lot to learn. For example, some species of the order have two cotyledons, and there is controversy about their nature and morphology. Again, the structure of the xylem- and phloem-

glomeruli in the nodes of the Dioscoreaceae seems to be unique in the monocotyledons; these glomeruli are well described by the author, who suggests that their functional significance should be investigated. At the end of Part I there is a valuable short chapter on general taxonomic conclusions based on anatomical evidence, but taking into account other evidence as well; and it is shown that anatomical characters have significance at family, genus and section levels.

In Part II, the families, genera and, in *Dioscorea*, the subgenera and sections are systematically described. The many line-drawings in the text-figures are carefully executed, but in many cases, where a whole vascular bundle is illustrated at a magnification of $\times 185$, the cells of the ground tissue are so tiny that they can hardly be clearly shown; and one wonders if diagrammatic representation would not have been better. Some of the sections in the photographs, too, are darkly stained and present a rather muddy appearance.

The book is well printed, though a line of text seems to be missing at the bottom of page 2. There is a good index. D. H. VALENTINE

Coping with Heat

The Stress of Hot Environments. By D. McK. Kerslake. Pp. x+316. (Cambridge University: London, May 1972.) £6; \$19.50.

A TEXT taking a long cool look at the physical and physiological basis of thermal stress indices has been long overdue and Dr Kerslake is undoubtedly one of the most suited for such a task. Taking the basic physical data concerning heat exchange between the body and its environment, the physiological data relating to heat transfer within the body and the production of sweat, Kerslake builds up a detailed theory of heat stress against which to compare a number of well known indices. The author does not spare the reader, there are no wasted words, the mathematics is copious and the continual development of ideas requires the reader's full attention. The book is written in a clear style developing concepts in easily grasped steps which should enable all to follow. The twenty-two pages of references, an index and the use of SI units throughout make it a useful reference book.

The first four chapters cover heat transfer and the heat balance of the sweating skin. The development of mean heat exchange coefficients for convection and evaporation is undertaken with detailed reference to the literature and their treatment, and that of radiant heat transfer, should motivate many

physiologists to examine their ideas in this area. In radiant heat transfer calculations it seems to be common practice to use the first instead of the fourth power relation, a procedure which is difficult to justify on the grounds of simplifying the calculations as the fourth power can be handled with logarithms or the calculations quickly done using a radiation slide rule. Kerslake examines the simplification and puts its use into perspective, namely to facilitate the joint treatment of radiation and convective heat exchange and the derivation of an operative temperature. Correctly done, making the radiant heat transfer equation linear is by no means a simplification.

The factors which influence and modify the heat exchanges of the body and have to be considered in the development of thermal indices, clothing, respiratory loss and the physiological responses are then covered. In considering the regulation of body temperature, Marius Nielsen's work of 1938 is quoted as proposing that the setting of the body's thermostat, that is, control mechanism, depends on the rate of work. This over-simple thermostat resetting approach to temperature regulation serves only to confuse and it is time it was buried.

The development of temperature regulation follows the normal pattern apart from the idea that heat flow itself may be monitored. This concept is brought in to explain similar sweat rates observed in stepwise increments of radiant heat load and sinusoidal radiant heat loads of progressively larger amplitude to match the values used in the steps. In view of the differences in the rates of change and absolute values of skin temperature in the two situations, this is insufficient reason for proposing the regulation of heat loss.

Having covered the basic groundwork the author sets about integrating the data and reducing the various components which contribute to thermal stress to lines of equal sweat rate (isohids) on a psychrometric chart. The isohids are then used to evaluate some of the commonly used indices. The final chapter covers storage limited heat exposure.

The virtue of the book is the detailed physical analysis of the heat exchanges between man and his environment; its weakness is that the manuscript was finalized at the end of 1970 just about the time P. O. Fanger published his book on thermal comfort and before the 1971 International Symposium on Environmental Physiology. Both events date the book and it is a pity Kerslake did not devote a few pages to a consideration of Fanger's comfort equation. Nevertheless, an excellent book and one to be recommended to all environmental physiologists.

G. W. CROCKFORD

CORRESPONDENCE

Siding Spring

SIR,—In his letter (*Nature*, **239**, 117; 1972), Professor Geoffrey Burbidge raises a number of issues on most of which I would not presume to comment. His points 3 and 5, however, with the strong implication that Siding Spring Observatory is an "inferior site" do concern this school and should not be allowed to stand. In addition, his assertion that a thorough assessment of observing conditions was not undertaken in choosing the location of the new observatory is not correct. The facts of the situation are as follows.

In the mid-1950s it became apparent that the Mount Stromlo Observatory, 12 miles from Canberra, would begin to lose effectiveness as the city grew. The Australian National University's Department of Astronomy, at that time under Professor B. J. Bok, therefore initiated a programme to find a better site, preferably (for logistical reasons) close to Canberra. A second objective, without the qualification, was to seek the best possible site in Australia for a large telescope. A wide ranging, site-testing programme was initiated over the period 1958-64, a total of fifteen sites being considered. The staff involved at the Australian National University were Professor B. J. Bok and Drs A. R. Hogg, S. C. B. Gascoigne, A. Rodgers and B. Westerlund. Night time cloud cover led to elimination of eleven sites and four years of detailed testing yielded the information shown in Table 1.

ment that Siding Spring Observatory was as good a site as was available in Australia at which to build a large telescope. This committee recommended that, if such an instrument was built, it should be at Siding Spring.

Experience at Siding Spring Observatory shows the atmosphere above it to be very transparent, with a visual atmospheric extinction coefficient of some 0.16 magnitudes per unit air mass. The seeing is good—the Australian National University 40-inch telescope has produced plates showing images as small as 0.5 arc s diameter. This is a good deal better than our Mt Stromlo Observatory, which at least one experienced US observer has stated to be as good as Mt Wilson.

Although comparisons can be misleading, the evidence available to us is that the Siding Spring Observatory site has characteristics very similar to Kitt Peak National Observatory in Arizona, where a 150-inch telescope, also, is in course of erection.

Sites in northern Chile certainly have one major advantage over both Siding Spring Observatory and Kitt Peak National Observatory, in that the usable time appears to be in the range of 80-85% as compared with some 60%. Chilean sites, however, have some disadvantages. They are remote from centres of learning and technology, they lie in an earthquake zone, and costs of building and operating highly sophisticated equipment are high.

The Australian National University

A Counter-homily

SIR,—On August 4, your leading article "Homilies for the Club of Rome" sounded off with "Earlier this year the organization which calls itself the Club of Rome achieved a notable publishing success . . .", thus putting the whole thing firmly on a commercial, return-on-capital basis. Now the organization which calls itself, and is, the Club of Rome is not just a bunch of eco-nuts or doomster-nuts. They are mainly people in positions in industry, banking and administration unlikely to be achieved by the soft-headed—Rectors or Vice-Chancellors of one or two Universities, Presidents of the Banque de Bruxelles and the Credit Lyonnais, Presidents or Chairmen of companies like Nippon Electric, Hitachi, Imperial Oil, and the Pulp and Paper Research Institute of Canada.

On the substance of what you adduce against the MIT simulation-model, Oerlemans, Tellings and de Vries (*Nature*, **238**, 251; 1972) point out that if you modify the MIT model by inserting an optimistic estimate of the effectiveness of discovery of new natural resources, the unfortunate effects of resource exhaustion would be averted. Boyd (*Science*, **177**, 516; 1972) shows that you can achieve an equally happy result if you insert a technology joker, which invents new methods (and, it is implied, delivers the goods on time) just enough to get over any sticky patches. All of which merely shows that the MIT model is a reasonably flexible system, capable of producing a coherent output when fed with a wide variety of inputs—whether garbage or not.

So what would I, as a member of the Club of Rome, bloody but unbowed under *Nature's* homilies, claim that the MIT team had contributed?

Not predictions of what will happen. They explicitly state that their results are not—repeat not—and they repeat it three or four times—predictions. It is really too obviously a setting up of straw men to criticize the outputs as though they were supposed to be forecasts of what will happen. The nearest they come to this is that they show what could happen if a set of trends, adjusted so that they at least fit the data from the last few decades, continue unmodified into the future. The catastrophes expressed in the MIT graphs are at least rationally conceivable; they are amongst the "possibles" we have to take into consideration.

Table 1 Results of Site-Testing

	Time usable completely photometric (%)	Time usable spectrophotometric (%)
Siding Spring Observatory (NSW)	43	63
Mt Serle (SA Flinders Range)	45	66
Mt Singleton (WA)	39	61
Mt Bingar (NSW)	44	65
Mt Stromlo Observatory (ACT)	27	48

In the event the university, after consideration of these data and other desirable features, chose to site its new observatory on Siding Spring Mountain. Since then the accuracy of the site assessment has been fully confirmed by seven years of operations at the observatory.

Later a local committee, comprising Drs R. Giovanelli (CSIRO), Harley Wood (NSW Government Astronomer), A. Rodgers (ANU) and W. C. Swinbank (CSIRO), who were given access to all the data, made the independent assess-

ment has been delighted to provide sites both for the SRC 48-inch Schmidt telescope and the Anglo-Australian 150-inch telescope at its Siding Spring Observatory.

We believe that work with these two first-class instruments, when they are completed, will make major contributions to astronomy in the future.

Yours faithfully,

E. W. TITTERTON

Research School of Physical Sciences,
Australian National University,
Canberra, ACT

Then they have demonstrated a point which people often accept in theory but forget when it comes to practice; that complex systems often react to inputs in unexpected and unintended ways. If you kick a black-box—an outboard motor that won't start, or a TV set—it may do better than before, if it has been designed to have good stability for its main function. But it may do something quite unexpected if its performance has not been well stabilized.

Thirdly, the MIT group have started what will clearly be a long-enduring process of modelling the global situation. Improvements on their Mark I scheme are obviously called for, and some are already in hand by groups associated with the Club of Rome. One American-German team is developing a model which will "dis-aggregate" the world into three sections: rich capitalist, communist, and the Third World. They will also add another level to the system, namely of goal-setting activities which attempt to control the causal mechanisms so as to attain certain objectives. Another South American group is particularly concerned to distinguish the rich and the poor regions and study the interactions between them.

Beyond these developments, there are three others which seem to me especially desirable: (i) a distinction between material products which are generally agreed to be socially desirable, for example, food and housing and so on for an increasing population, and products which are unnecessary or undesirable (electric toothbrushes, arms); (ii) a recognition of the place of tertiary and quaternary employment (services, information processing, including education); (iii) allowance for unavoidable time lags (how long will it

take for increased investment in agriculture or natural resource utilization actually to produce and distribute fertilizers, say, or an infra-structure of roads, bridges and so on?).

There is no reason why such factors should not be built into later versions of world models, and I suggest they almost certainly will be. *Nature* ends its homily by telling the Club of Rome that it will have to live with some modifications of the Mark I model, exhibiting different properties. I think the remark boomerangs. *Nature* will find that it has to live with a new field of computer-model exploration of the world system, perhaps comparable in activity to the fields of computer exploration of intelligence and language.

Yours faithfully,

C. H. WADDINGTON

*Department of Genetics,
University of Edinburgh*

Postcards to *Nature*?

SIR,—Professor McCrea's suggestion (*Nature*, 239, 239; 1972) for author credit, refereeing and editing seems likely to generate more editing on your part than it will save, if your correspondents write to point out the many flaws of the idea. May I therefore refrain from criticism and offer instead an alternative scheme?

Basically my suggestion is that journals should publish in full only those papers for which there is a proven demand. The existence of such a demand could be assessed by the initial publication of the abstract alone. Proof of a readership would then be the receipt, within some specified period, of

an adequate volume of requests for further details; the time allowed would clearly vary from subject to subject and journal to journal. If the number of requests received were large enough the full paper would be refereed, edited and published as at present, thus taking its deserved place in the scientific literature; otherwise it would be the responsibility of the author to send photocopies or the like of his manuscript to those few people who had requested details of the work.

In some subjects the delay involved in the process described above would be undesirable. In most of these subjects, however, there will be considerable personal contact between those engaged in the field and it should be possible for an author to demonstrate the existence of a readership when submitting his manuscript to the journal; the paper could then be published forthwith.

Some people may object that many of the papers published in *Nature* are already so short that their abstracting would cause difficulty. Logically, however, this problem should be met by requiring very short abstracts with which to test for a readership; perhaps these could be published as "Postcards to *Nature*"?

Both Professor McCrea's suggestion and my own are based on the assumption that scientists currently write too much about too little, thus clogging the literature with print few wish to read; in this case one may well ask whether the solution does not lie in more (and more stringent) refereeing rather than in less!

Yours faithfully,

RAYMOND J. O'CONNOR

*Department of Zoology,
The Queen's University of Belfast,
Belfast BT7 1NN*

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